STUDIES IN SOLVOLYSIS OF SOME SIMPLE ALKYL TRIFLUOROACETATES

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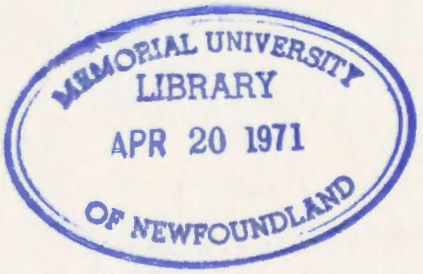
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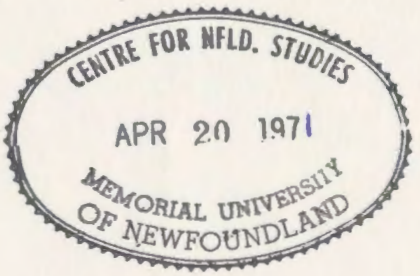
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STUDIES IN SOLVOLYSIS OF SOME SIMPLE ALKYL TRIFLUOROACETATES

A Thesis

by

Sheila T. Lobo, B. Sc.

Submitted in partial fulfilment
for the degree of Master of Science.

Memorial University
of Newfoundland

February, 1970

ACKNOWLEDGEMENTS

The author wishes to express sincere thanks to Dr. J. M. W. Scott for guidance throughout this work, to Technical Services of Memorial University for their assistance, to Memorial University for financial support and finally to Mrs. R. Hunt for typing the thesis.

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ABSTRACT

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The work presented in this thesis, deals with the neutral hydrolysis of simple alkyl trifluoroacetates. The alkyl trifluoroacetates CF_3COOR [R = CH_3, $-CD_3$; $-CH_2CH_3$, $-CD_2CD_3$; $-CH(CH_3)_2$, $-CH(CD_3)_2$ and $-C(CH_3)_3$] have been synthesized. The rates of hydrolysis of these trifluoroacetates have been measured at various temperatures, by a conductimetric method, and the thermodynamic parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) evaluated. Secondary deuterium isotope effects have been determined. The results have been interpreted in the light of other mechanistic information concerning the hydrolysis of simple haloacetates.

INTRODUCTION

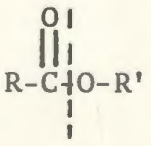
INTRODUCTION

Winter (1) has studied the temperature dependence of the rates of neutral hydrolyses of a series of alkyl trifluoroacetates (CF_3COOR; R = Me, Et, i-Pr, t-Bu) in H_2O and D_2O. From the solvent isotope effects (SIE) and enthalpies, entropies and heat capacities that characterize the activation process for these compounds, it was concluded that the methyl and ethyl esters react by a '$B_{AC}2$' acyl-oxygen fission mechanism.

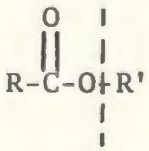
At this juncture, it is best to review the mechanistic classifications for ester hydrolysis and the meaning of the designation '$B_{AC}2$' in particular.

Esters may be hydrolysed by acids or alkalies and there are many instances cited in the literature to convince us of the different mechanisms that apply in these two cases. Neutral hydrolysis (with which we are concerned in the present study) is not so well documented and it "can be shown to be more than a simple extrapolation of the alkaline and acid reactions." (2) In principle, the cleavage of an ester could occur in two different places (a) between the acyl group and the oxygen atom (acyl-oxygen fission), (b) between the alkyl group and the oxygen atom (alkyl oxygen fission)

(a)



(b)



Acyl-oxygen fission is most common, although alkyl-oxygen fission may occur in favourable circumstances.

Day and Ingold (3) used three criteria in their ester hydrolyses classification scheme (a) kind of catalysis, (b) kind of fission, (c) molecularity of the reaction. On these criteria, there are eight mechanistic divisions, six of which have been experimentally identified. $B_{AC}1$ and $A_{AC}2$ mechanisms have not been observed. The classification scheme is shown in Table I.

TABLE I

CLASSIFICATION OF ESTER HYDROLYSIS REACTIONS

Basic Catalysis	Acidic Catalysis
Acyl Fission	Acyl Fission
Monomolecular	Monomolecular
Bimolecular	Bimolecular
Alkyl Fission	Alkyl Fission
Monomolecular	Monomolecular
Bimolecular	Bimolecular

The letter 'B' is used to represent "basic" mechanisms, which include both neutral and alkaline hydrolyses, and the letter 'A' represents the acidic mechanism. 'AC' and 'AL' designate acyl and alkyl oxygen fissions, respectively. Numbers 1 and 2 indicate whether the reaction

is uni- or bimolecular in the rate-determining step. Thus, '$B_{AC}2$' represents base catalysed hydrolysis reaction which undergoes acyl-oxygen fission, and which is bimolecular in the rate-determining step. It is obvious, now, why the '$B_{AC}2$' description for the mechanism of neutral hydrolysis of trifluoroacetates is inadequate, at least until the probable course of the over-all process is specified in detail.

Thus, the acid catalysed hydrolyses are $A_{AC}1$, $A_{AC}2$, $A_{AL}1$ and $A_{AL}2$. The $A_{AC}2$ and $A_{AC}1$ mechanisms are also called A2 and A1 respectively. Both $A_{AC}1$ and $A_{AC}2$ mechanisms involve a pre-equilibrium with the addition of a proton. In the $A_{AL}1$ mechanism, a rate-controlling heterolytic fission occurs, which produces a carbonium ion, which is then rapidly attacked by the nucleophile, resembling an S_N1 reaction. In the $A_{AC}2$ mechanism, there is a slow reversible attack of water molecule. The $A_{AL}1$ mechanism occurs most readily when the alkyl group comes off as a stable carbonium ion.

Considering the basic catalysed hydrolyses, the $B_{AC}2$ mechanism occurs most frequently. The $B_{AL}2$ mechanism is very rare and is formulated as follows (2):

$$H_2O + R\text{-}OC.O.R' \underset{\text{slow}}{\overset{\text{slow}}{\rightleftharpoons}} \overset{+}{H_2}OR + \overset{-}{O}.CO.R'$$

$$R.\overset{+}{O}H_2 + \overset{-}{O}.CO.R' \xrightarrow{\text{fast}} ROH + HO.CO.R'$$

It has been observed in the hydrolysis of β-lactones (4) and the alkaline hydrolysis of methyl-2, 4, 6 tritert-butyl benzoate (5), to mention some among the very few.

The carboxylic ester molecule contains two positions susceptible to nucleophilic attack viz. the carboxyl carbon atom and the α-carbon atom of the alkyl group. Unsaturation, in the carbonyl carbon, makes it more favorable for attack by a nucleophile. Hence, it is possible that both acyl-oxygen and alkyl-oxygen fission occur simultaneously although the former is faster and predominates and is, therefore, the only observable process. However, in the appropriate solvent, such as neutral water or weakly alkaline solutions, it is possible to observe the $B_{AL}1$ mechanism. This mechanism is formulated as follows (2):

$$R\text{-}O\text{-}CO.R' \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} R^{+} + \bar{O}.CO.R'$$

$$R^{+} + OH_2 \underset{\text{slow}}{\overset{\text{fast}}{\rightleftharpoons}} R - \overset{+}{O}H_2$$

$$R.\overset{+}{O}H_2 + \bar{O}.CO.R' \xrightarrow{\text{fast}} ROH + HO.CO.R'$$

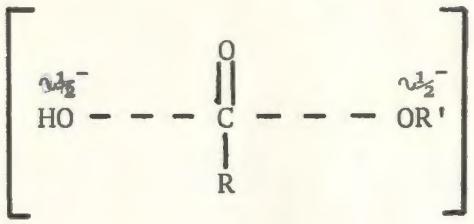
The $B_{AC}2$ mechanism is kinetically second order; first order in ester and first order in OH^-, if OH^- is the nucleophile used. The mechanism established by Bender (6) from a study of the alkaline hydrolysis of three different esters viz. ethyl, isopropyl and t-butyl benzoates is written below:

$$OH^- + \underset{R}{\overset{O}{\overset{\|}{C}}}\text{-}OR' \underset{\text{slow}}{\overset{\text{slow}}{\rightleftharpoons}} \left[HO\text{----} \underset{R}{\overset{O}{\overset{\|}{C}}} \text{-----} OR' \right]^{-} \underset{\text{slow}}{\overset{\text{slow}}{\rightleftharpoons}} HO\text{-}\underset{R}{\overset{O}{\overset{\|}{C}}} + OR'^{-}$$

I

$$\xrightarrow{\text{fast}} RCO_2^- + R'OH.$$

The intermediate I can be written (3) in the form



Considering the structural effects on the rate of hydrolysis of esters by a $B_{AC}2$ mechanism, it can be concluded that electropositive substituents retard and electronegative substituents accelerate the reaction, since the intermediate is negatively charged. Also, the reaction being akin to the S_N2 reaction, steric effects play an important role in determining the rate of hydrolysis.

With an ester RCOOR' (R = Me, Et etc.) the rate of hydrolysis is very dependent upon the part played by R in decreasing the availability of electron supply at the seat of the reaction. If the hydrogen atoms are replaced by fluorine atoms, R withdraws electrons efficiently, which decreases the ability of an ester to accept protons and increases the tendency for a water molecule to combine with the carbonyl carbon atom (7). With most carboxylic esters, the reaction with water is of subordinate importance compared with the acid or base-catalysed hydrolysis. For esters of stronger acids, the reaction with water becomes more important and the acid catalysed reaction becomes negligible (7). Trifluoroacetic acid is very much stronger than other carboxylic acids, because of the powerful electron attraction by the three fluorine atoms, and it is largely dissociated in dilute solution in water. Also it is not so bulky a group as to offer steric hindrance to the approach of a water molecule to the reaction site. Hence, esters of trifluoroacetic acid seem to offer

an ideal opportunity to study the spontaneous neutral hydrolysis in water by a $B_{AC}2$ mechanism.

A wide literature survey has been done by Winter (1), with regard to ester hydrolysis in general and halogenoacetates in particular. Hence mention will be made only of the highlights pertaining to halogenoacetates in the past twenty years.

Bender (8) has written an extensive review on the catalytic aspects of the mechanisms of reaction of carboxylic acid derivatives, limited to those reactions of carboxylic acid derivatives which occur with acyl-oxygen fission. In aqueous solutions which, of course, contain hydronium ions, hydroxide ions and water, the general expression for the observed velocity constant of a hydrolytic reaction is:

$$k = k_o + k_a [H_3O^+] + k_b [OH^-] \qquad (1)$$

where,

k_o = specific rate constant for the "spontaneous" or neutral hydrolysis of the ester.

k_a = specific rate constant for the acid catalysed process of the reaction.

k_b = specific rate constant for the base catalysed process of the reaction

Since,

$$K_w \text{ [dissociation constant for } H_2O] = [OH^-] [H_3O^+],$$

the above equation can be written as

$$k = k_o + k_a [H_3O^+] + \frac{k_b \cdot K_w}{[H_3O^+]} \qquad (2)$$

As noted by Winter (1) since there is no autocatalysis by trifluoroacetic acid in the solvolysis of trifluoroacetates over 93.3% of the reaction, k_o is the rate constant that really matters in the present study. Extensive work has been done in the fields of acid and base catalysed halogenoacetates hydrolyses reactions (i.e. in determining k_a and k_b) but not too much stress has been laid on the neutral hydrolyses of the system. A few of the important examples on neutral hydrolysis, especially of halogenoacetates, will be cited below.

In the late fifties, Moffat and Hunt published work on hydrolysis of fluorinated esters--effects of substituents, solvents and chain lengths on rates of hydrolyses of these esters (9), (10), (11). The object of (9) was to determine the effect of chain-length of both the acid and the alcohol component upon neutral hydrolysis of n-alkyl esters of perfluorinated acids. All of the reactions were found to be pseudo-first order. They observed that the hydrolysis rate constants for the n-alkyltrifluoroacetates levelled off rapidly with increasing chain length, which parallels Tommila's observation (12) on the alkaline hydrolysis of n-alkyl benzoates. They related the hydrolysis rate constants for the n-alkyl trifluoroacetates in acetone-water solutions to the structure of n-alkyl group by

$$\ln k = \frac{a}{M} + b \qquad (3)$$

where a, b are constants and M is the molecular weight of R in

CF_3CO_2R. This equation leads to,

$$\log \frac{k}{k_o} = a(M_o - M)/2.303\ M_oM \qquad (4)$$

which is similar to Taft's equation (13)

$$\log \frac{k}{k_o} = fA \qquad (5)$$

where M_o is the molecular weight for the standard R in CF_3COOR viz. CH_3-; M is the molecular weight of R for the compound considered; k_o is the rate constant for the standard (methyl ester) in the series, k is the rate constant for the compound in question; f depends upon the nature of the reaction series and A is a substituent constant, dependent upon the nature of the substituent for each set of reaction series. One series is defined as a standard, which implies that the value of the constant for that series is unity. If equation (4) and (5) are identical, then equation (4) can be used to calculate absolute values for f and A. If for n-alkyl benzoates, f = 1

then,

$$A = a(M_o - M)/2.303\ M_oM \qquad (6)$$

Moffatt and Hunt observed that the A's calculated by equation (6) were in agreement with those calculated by Taft (13).

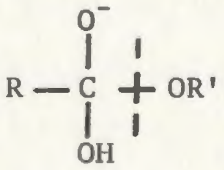
Hughes and Ingold (14) had proposed a slow formation of a carbonium ion for the hydrolysis of tertiary alkyl chlorides. On hydrolysing tertiary alkyl trifluoroacetates in a mixture of acetone (70% by volume) and water, Moffatt and Hunt (10) found first order reactions. The enthalpies and entropies of the activation (E in the

region of 24 kcals/mole and $\Delta S^{\ddagger}$ in the region of -3 to -4 e.u.) and percentage elimination of olefin seemed to indicate a reaction involving the slow formation of a carbonium ion and then S_N1 - S_N2 mechanism.* They proposed

$$CF_3CO_2R \longrightarrow CF_3CO_2^- + R^+ \qquad (7)$$

as the slow step in the hydrolysis of t-alkyl trifluoroacetates.

Moffatt and Hunt (11) investigated the effect of chain-length upon the rates of hydrolysis of sec-alkyltrifluoroacetates and the effect of increasing the water concentration of the solvent (10) on the rates of uncatalysed hydrolyses of primary and secondary alkyl trifluoroacetates. The effects of aryl groups upon the non-catalysed hydrolysis of some aryl trifluoroacetates were also investigated. They tried to account for the very large differences observed between acid-catalysed and base catalysed aryl oxygen cleavage as far as chain-length effects and solvent effects were concerned. They attempted to relate chain-length effects and reactivity through a function of the reciprocal of the mass of the intermediate involved. The intermediate is written below:



μ the reduced mass is $\frac{M_1M_2}{M_1 + M_2}$, where M_1 is the mass of the group to the left of the bond that is broken and M_2 is the mass of the - OR' group. The relation between the rate of hydrolysis and the reduced mass is,

$$\ln k = \frac{a}{\mu} + b$$

---

*For terminology of S_N1 - S_N2 mechanism, see Ref. 1, pg. 27.

where a and b are constants; k is the rate constant. From plots of logk vs $\frac{1}{\mu}$ the applicability of the equation seemed valid for the secondary alkyl trifluoroacetates and benzoates.

Euranto et. al. (15), (16), (17) have been steadily working on acid-catalysed, base-catalysed and neutral hydrolyses of haloacetates. Euranto and Cleve (15) investigated the hydrolysis of the methyl ester of monochloroacetic acid in 1:1 (by weight) methylacetate-water mixtures and that of the methyl ester of dichloroacetic acid in water. In the latter case they observed autocatalysis by acid liberated during the hydrolysis. The ionisation constant of dichloroacetic acid was measured from $5^{o}C$ to $85^{o}C$ to correct for the autocatalysis and ΔC_p of activation was found to be -52.7 ± 6.0 cals/mole/^{o}C which is similar to that found by Scott and Winter (1) for ethyl trifluoroacetate.

In the hydrolysis of chloromethyl chloroacetate (16) in H_2O followed by argentometric method, the heat capacity of activation at $25^{o}C$ was found to be -40 cals/mole/^{o}C and the heat and entropy of activation were 11.8 kcals/mole and -37 e.u. respectively. Addition of neutral salts like NaCl and $NaClO_4$ were found to retard the reaction strongly, and acids like HCl and $HClO_4$, on the contrary increased the rate of hydrolysis. Euranto and Cleve (16) proposed that the neutral hydrolysis of chloromethyl chloroacetate proceeds by the $B_{AC}2$ mechanism of the alkaline ester hydrolysis, so modified that the attacking species is a water molecule rather than a hydroxyl ion.

More recently Euranto (18) has surveyed the hydrolyses of α-halosec-alkyl esters in water-acetone mixtures. The kinetic data for

α-chloroisopropyl trichloroacetate [$CCl_3COOCCl(CH_3)_2$] clearly deviate from those of the other α-chloroisopropyl esters studied. The exceptionally low values for the Arrhenius parameters and the activation enthalpy and entropy [in 80% (volume) acetone-water, $\Delta H^{\ddagger}$ is 8.91 kcals/mole and $\Delta S^{\ddagger}$ = -50.3 e.u.] indicate that the hydrolysis of α-chloroisopropyl trichloroacetate does not take place as a displacement of chlorine, but as a neutral hydrolysis by the $B_{AC}2$ mechanism like that of many other esters with electronegative substituents (19). Euranto observed that when the structure R' of a α-chloroisopropyl ester [$R'COOCCl(CH_3)_2$] is varied, electropositive groups increase the rate, k_{Et}/k_{Me} = 1.4 and electronegative groups reduce it strongly $k_{CCl_3}/k_{Me} < 10^{-3}$; the rate of S_N1 solvolysis of α-chloroisopropyl trichloroacetate was found to be only a small fraction of the observed rate. These effects are similar to those found for α-chloroethyl esters [$R'COOCHClCH_3$] - k_{Et}/k_{Me} = 1.3; k_{CH_2Cl}/k_{Me} = 0.012 (20).

Tracer experiments have provided the most direct evidence for acyl-oxygen fission in reactions of carboxylic acid derivatives. Polanyi and Szabo (21) observed in the saponification of n-amyl acetate in H_2O^{18}, that the amyl alcohol produced was isotopically normal. Thus they concluded that acyl-oxygen fission had occurred.

$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}O\text{-}R' + H_2O^{18} \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}O^{18}\text{-}H + R'\text{-}OH \qquad (9)$$

This conclusion is correct, but it has been pointed out (8) that the original evidence is probably meaningless, because the method of isotopic analysis involved a step where oxygen could be lost.

Bunton et. al. (22), (23), (24), (25), (26), (27) have used the tracer technique, as a very sensitive criterion of bond fission in ester hydrolysis, be it acid-catalysed, base-catalysed or neutral hydrolysis. The reactions are usually carried out with water enriched in ^{18}O and the position of bond fission was directly given by isotopic analysis of the products. Of particular interest, in the present work, is the study of the hydrolysis of methyl trifluoroacetate by Bunton and Hadwick (23). Through their tracer studies, they found that the hydrolysis of methyl trifluoroacetate in water and dioxan-water 60:40 (v/v), the acyl-oxygen bond was broken. The addition of alkali had a marked effect on the hydrolysis. This shows that the mechanism involved is $B_{AC}2$. The fact that the Arrhenius parameters were in the range usually associated with bimolecular ester hydrolyses by acyl-oxygen fission and that the rate increased with increasing water content of solvent, provided sufficient evidence that the nucleophilic attack of a water molecule on the acyl carbon was the slow step in this $B_{AC}2$ mechanism. Of course, whether the bond-making and -breaking were synchronous or whether a stable intermediate was formed by nucleophilic addition to the acyl-carbon of the ester was not known.

An interesting piece of work was done recently on the spontaneous hydrolysis of some trichloroacetates (28). Talvik and Heinloo (28) measured the rates of spontaneous hydrolysis of CCl_3COOMe, CCl_3COOEt and $CCl_3COOiPr$ in aqueous solution at 60^oC, using both spectrophotometric and conductometric methods. A plot of $\log k_o$ vs E_s^o [steric constant of the alkyl group R' = Me, Et, iPr] yielded a linear plot, indicating a $B_{AC}2$ mechanism for the neutral hydrolysis of these esters in water. Hence,

as the CF_3- group in the trifluoroacetates is slightly more electron-withdrawing than the CCl_3- group, one would expect a similar trend for the neutral hydrolysis of CF_3COOMe, CF_3COOEt, $CF_3COOiPr$ in water.

From what has been said so far, it seems that within the trifluoroacetate series there is a change in mechanism as one goes down the series Me, Et, iPr to tBu. The Moffatt and Hunt work together with Bunton's tracer studies on Me trifluoroacetates seem to indicate a $B_{AC}2$ mechanism for the primary and secondary ester hydrolyses (neutral and base-catalysed) and an S_N1-S_N2 mechanism for the tertiary ester hydrolysis. Also, the enthalpy of activation for the primary and secondary esters is in the region of 10 kcals/mole (9). The tertiary ester has an enthalpy of activation which is more positive by about 15 kcals/mole (10) and since it produces from 15-33% of elimination product, it is indicative of the slow formation of a carbonium ion intermediate (S_N2-S_N1? mechanism). Thus the thermodynamic parameters also seem to indicate a different mechanism for the tertiary ester from the primary and secondary esters.

Winter and Scott (29) attempted to locate the region of mechanistic change in the neutral hydrolysis of CF_3COOR (R = Me, Et, iPr, tBu) series by determining the thermodynamic parameters ($\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta Cp^{\ddagger}$) which characterize the activation process, and the solvent isotope effect of each of the esters in light and heavy water. Table II (29) shows the rate constants for the neutral hydrolyses of the trifluoroacetates at 4.98°C, 9.96°C and 14.95°C in light and heavy water, accompanied by the solvent isotope effects at these temperatures. Table III (29)

TABLE II

RATE CONSTANTS AND ISOTOPE EFFECTS FOR THE SOLVOLYSIS OF TRIFLUOROACETATES IN WATER AND DEUTERIUM OXIDE†

Ester	T°C	$k_{H_2O} \times 10^{4(n)*}$	$k_{D_2O} \times 10^{4(n)*}$	k_{H_2O}/k_{D_2O}
-Me	4.98	23.09 ± 0.10 (4)	6.486 ± 0.008 (4)	3.54
	9.96	32.80 ± 0.05 (4)	9.420 ± 0.027 (4)	3.51
	14.95	46.42 ± 0.13 (3)	13.24 ± 0.05 (4)	3.48
-Et	4.98	8.777 ± 0.026(4)	2.390 ± 0.009 (4)	3.67
	9.96	12.53 ± 0.04 (5)	3.468 ± 0.010 (4)	3.60
	14.95	17.57 ± 0.05 (4)	4.956 ± 0.017 (4)	3.54
-iPr	4.98	2.433 ± 0.008(4)	0.6339 ± 0.019 (4)	3.83
	9.96	3.494 ± 0.012(3)	0.9194 ± 0.028 (5)	3.79
	14.95	4.864 ± 0.022(4)	1.296 ± 0.002 (4)	3.74
-tBu	4.98	0.5723 ± 0.030(3)	0.4623 ± 0.030 (3)	1.24
	9.96	1.296 ± 0.004(4)	1.076 ± 0.008 (4)	1.21
	14.95	2.915 ± 0.012(3)	2.450 ± 0.007 (3)	1.19

† See Reference (29)

* (n) is the number of runs

TABLE III

THERMODYNAMIC PARAMETERS FOR THE SOLVOLYSIS OF TRIFLUOROACETATES IN WATER AND DEUTERIUM OXIDE (DERIVED FROM THE RATES REPORTED IN TABLE II)*

Ester	$\Delta H^{\ddagger}$ (H_2O) kcals/mole	$\Delta H^{\ddagger}$ (D_2O) kcals/mole	$\Delta S^{\ddagger}$ (H_2O) e.u.	$\Delta S^{\ddagger}$ (D_2O) e.u.
-Me	10.60 ± 0.03	10.48 ± 0.05	-32.3 ± 0.3	-34.0 ± 0.4
-Et	10.53 ± 0.03	11.08 ± 0.03	-34.5 ± 0.3	-35.1 ± 0.3
-s-Pr	10.51 ± 0.05	10.87 ± 0.05	-37.1 ± 0.6	-38.5 ± 0.7
-t-Bu	25.44 ± 0.06	26.08 ± 0.05	13.7 ± 0.5	15.5 ± 0.0

* See Reference (29)

contains the thermodynamic parameters for the hydrolysis in H_2O and D_2O.

Schalager and Long (30) have given mechanistic significance to $\Delta S^{\ddagger}$. According to them, a change in mechanism in a series of similar substrates is sometimes indicated by a difference in the entropy of activation. This is obvious from Table IV which reports $\Delta S^{\ddagger}$, $\Delta H^{\ddagger}$ values for reactions proceeding by a different mechanism viz $B_{AC}2$ and S_N1. Each have characteristic values for $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$.

The values for $\Delta S^{\ddagger}$ for the methyl, ethyl and isopropyl trifluoroacetates center around -35 e.u. (29) and their $\Delta H^{\ddagger}$ values are in the general region of 10.5 kcals/mole; but the tert-butyl trifluoroacetate shows a dramatic change in both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. Table III reports a $\Delta H^{\ddagger}$ value which is 15 kcals/mole higher than the other three esters and $\Delta S^{\ddagger}$ which is ca. 50 e.u.'s more positive. These differences in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ seem to clearly point out a mechanistic change in the series. The actual magnitude of the enthalpies and entropies of activation are comparable with thermodynamic parameters, which characterize these two mechanisms (cf. Table IV). Thus on the basis of the tracer work by Bunton et al. (23) and the work by Moffatt and Hunt (9), (10), (11) together with the survey on the thermodynamic parameters, the methyl, ethyl and isopropyl trifluoroacetates react by a $B_{AC}2$ mechanism and the tert-butyl ester by an S_N1 mechanism. However, there is a possibility that the tertiary ester may be reacting by a mixed $B_{AC}2$ - S_N1 mechanism.

The solvent isotope effect in Table III did not help in distinguishing between the S_N2 and S_N1 mechanism. The value of 1.2 for the tertiary ester as compared to the value of 3.5 - 3.8 for the primary and secondary esters, supported the fact of the change in mechanism down

TABLE IV

SOME TYPICAL VALUES OF $\Delta S^{\ddagger}$ AND $\Delta H^{\ddagger}$ PARAMETERS FOR NEUTRAL HYDROLYSIS

Type	Compound	T°C	$\Delta H^{\ddagger}$ kcalmole^{-1}	$\Delta S^{\ddagger}$ Cal.mole^{-1}deg^{-1}	Reference
S_N1	tert-butyl chloride	10	23.80	14.4	(31)
S_N1	tert-pentylchloride	10	21.98	10.2	(32)
(?)	α-bromoisobutyrate ion	25	28.96	20.6	(33)
$B_{AC}2$	Methylchloroformate	25	16.199	-19.07	(34)
S_N1	Isopropylchloroformate	25	24.102	10.12	(34)
$B_{AC}2$	α-chloroisopropyl trichloroacetate	35	8.91	-50.3	(18)
$B_{AC}2$	chloromethylchloro acetate	25	11.8	-37.0	(16)

the trifluoroacetate series. Bunton and Shiner (35) have predicted on the basis of a zero-point energy model, solvent isotope effect (S.I.E.) values of 3.4 ~ 3.8 for primary and secondary ester hydrolyses. This treatment, according to Winter and Scott (29), is oversimplified. The value of 1.2 for the tertiary ester is typical of a reaction proceeding by S_N1 - S_N2 mechanism studied by Laughton and Robertson (36), (37), (38), (39). All that could be concluded from the solvent isotope effect study was that the S.I.E. substantiated the mechanistic classification based on enthalpies and entropies of activation. A study of the heat capacity for the hydrolysis of ethyl trifluoroacetate produced a value of -66.99 cals/mole/deg. The magnitude of this parameter is consistent with the idea that the solvolytic process involves the formation of a highly polar transition state from an initially neutral substrate and that the solvent reorganisation brought about by the electric charges associated with the transition state is responsible for almost the entire value of $\Delta Cp^{\neq}$ (33), (40). Since there is enough evidence for the $B_{AC}2$ mechanism of the ethyl ester hydrolysis, the heat capacity of activation alone does not distinguish between the $B_{AC}2$ and S_N1 - S_N2 type mechanisms. But $\Delta Cp^{\neq}$ may distinguish between S_N1 - S_N2 and $B_{AC}2$ mechanisms within the series of trifluoroacetates.

The present investigation was undertaken with the view to substantiate the conclusions based on (a) thermodynamic parameters, and (b) S.I.E. Kinetic secondary isotope effects, in particular, have been the subject of intensive investigation during the past several years and seem to have attained the status of a mechanistic criterion. The

results of the effects of α- and β- deuterium substitution on the rates of solvolysis reactions have been analysed in terms of the Bigeleisen (41) or Melander (42) formulation for the effect of isotopic substitution on reaction rate. In this theory, as derived from Absolute Rate Theory and Statistical Mechanics, the isotope effect is quantitatively related to the molecular vibrational frequencies of the initial and transition states for the protium and deuterium compounds.

The deuterium isotope effect may be understood qualitatively by taking a very naive view of it. The zero-point energy differences of hydrogen and deuterium probably contribute the most to the isotope effect. Consider an example in which the hydrogen is attached to a fairly heavy carbon containing residue and that the C-H bond is weakened in the transition state. Using the Infinite Mass Diatomic Oscillator approximation and the Born-Oppenheimer principle, the Bigeleisen equation (41), (43) reduces to

$$k_H/k_D = \exp\left[\frac{hc}{2kT}(\Delta\nu_H - \Delta\nu_D)\right] \qquad (10)$$

where $\Delta\nu_H$ and $\Delta\nu_D$ are the changes in going from the initial state to the transition state, h is Planck's constant, c is the velocity of light, k is Boltzmann's constant and T is the absolute temperature. The C-H and C-D bonds have essentially the same force constants in both states, but for a given change in the force constant of the C-H oscillator, because of its smaller reduced mass, it will suffer a greater change in frequency than the C-D bond. Hence $\Delta\nu_H > \Delta\nu_D$ and $k_H/k_D > 1$, according to equation (10). Since the C-H oscillator loses more zero-point energy in going to the transition state, the activation energy of the protium compound E_a^H is less

than that for the deuterium compound E_a^D (see Figure 1).

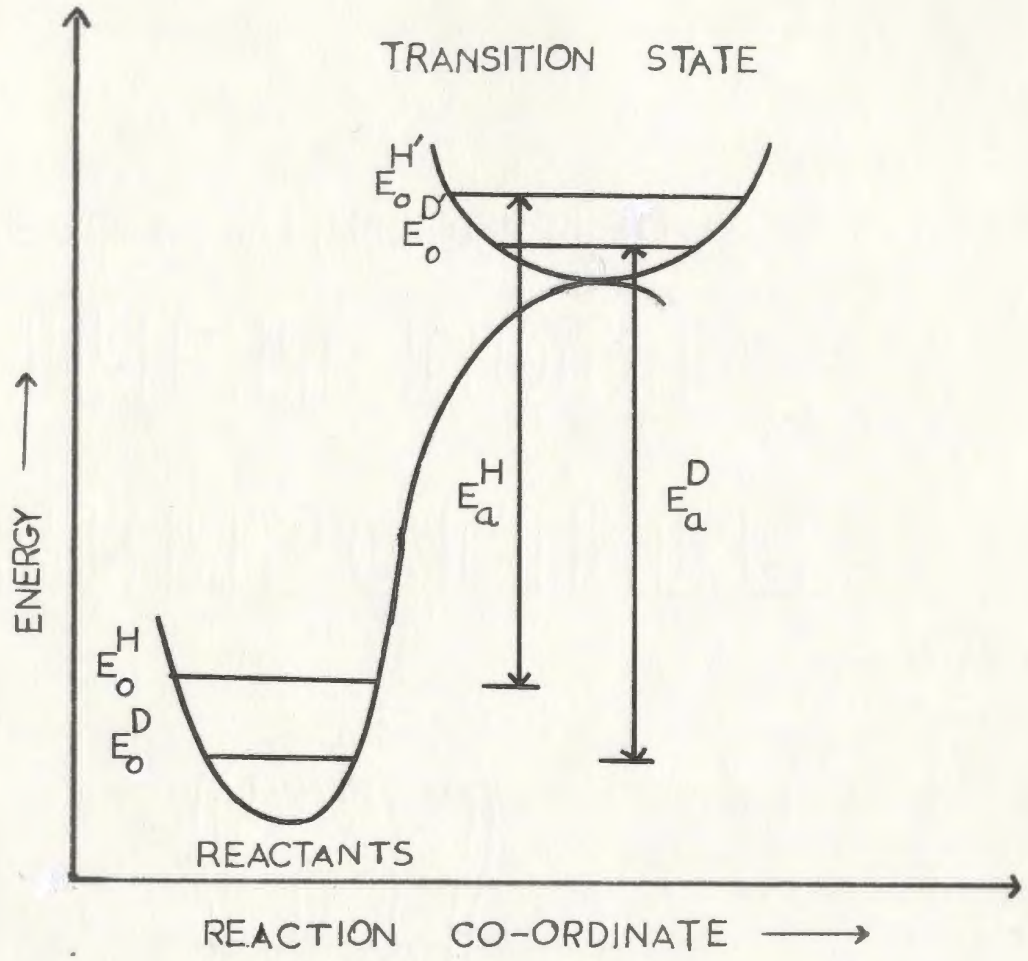


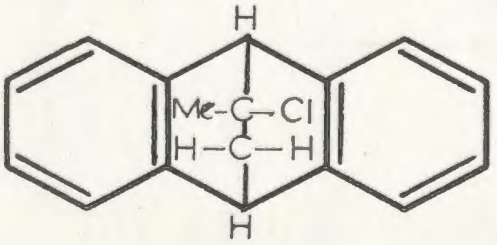
FIGURE 1.

Deuterium isotope effects (or any isotope effects for that matter) have been classified as primary and secondary. A primary effect occurs when the bond that is being ruptured in the rate-determining step, is isotopically substituted. Thus primary effects are large, sometimes of the order of 700%. Secondary isotope effects are effects on reaction rates and equilibria of isotopic substitutions, not directly involved in bond formation or bond rupture processes. The secondary isotope effects are further subdivided into those of the first kind and those

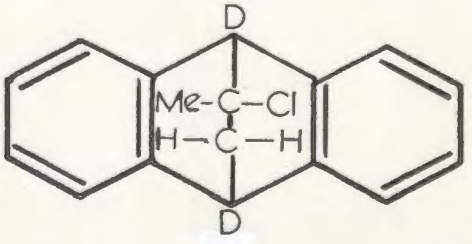
of the second kind, the criterion being whether or not bonds to isotopic atoms have undergone spatial reorientation (44). This definition differs from that of Streitwieser's, who ascribes the effects of the first kind to hybridisation changes and reserves the second kind for those effects "that behave like inductive effects." Halevi (44) feels that his classification scheme based on the presence or absence of significant structural changes in the region of isotopic substitution "is likely to survive longer than one based on theoretical concepts, no matter how well established these seem to be at the time."

It seems germane, at this stage, to discuss the origins of secondary deuterium isotope effects. The so-called secondary isotope effects were first detected in the kinetics of S_N1 solvolysis of compounds containing a β-deuterium atom (45), (46) independently by Lewis and Shiner. They attributed the cause to hyperconjugation effects. Since then, these workers and their groups have done extensive work, to establish steric effects, substituent effects and solvent effects on hyperconjugation (47), (48), (49), (50), (51), (52), (53), (54), (55), (56), (57), (58), (59), (60), (61), (62). The other effects are the usual electronic effects in organic chemistry--induction, hybridisation and steric interactions. Of course, there has been considerable discussion on whether hyperconjugation or induction is the source of secondary isotope effects, and here it is not proposed to establish the uniqueness of either viewpoint, but use each of these interpretations when appropriate to elucidate mechanisms.

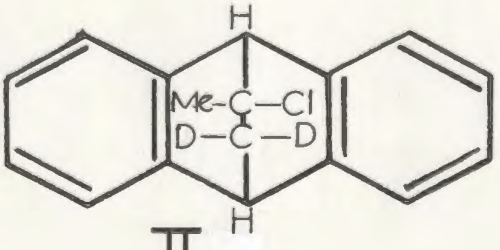
The work of Lewis and Shiner and their respective groups has established, that substitution of deuterium for protium in hyperconjugative positions usually produces kinetic isotope effects. The weakening of the C-H link, which is represented in valence bond theory by the contribution of non-bonded structures to the hybrid, is thought to decrease the zero-point energy by facilitating the vibrations, which involve relatively extensive movement of β-hydrogens. Shiner (62) has suggested that large secondary isotope effects caused by β-deuterium substitution are characteristic of a deuterium in a trans position to the leaving group in the transition state. The dependence of the isotope effect on the conformation of the molecule has been used as an argument against the postulate that steric isotope effects are the dominant influence on isotope effects. To prove his point that hyperconjugation is an important factor in solvolytic β-deuterium isotope effects, a striking example (49) is the solvolysis of compounds I, II and III in 60% ethanol at 45°C.



I



III



II

In this S_N1 solvolysis, the bridgehead carbon-hydrogen bond projects away from and is normal to the developing vacant p-orbital in the carbonium ion produced, while the hydrogens on the β-methylene are suitably situated for hyperconjugation with the reaction site. Thus, the results given in Table V are completely in accord with the hyperconjugative mechanism for the β-isotope effect. This point is supported by the

TABLE V

FIRST ORDER RATE CONSTANTS (49)

Compound	$k \times 10^5$ sec^{-1}	k_H/k_D
I	8.99	--
II	7.92	1.14 ± 0.01
III	9.12	0.986 ± 0.01

fact that any change in the electron deficiency on the carbon at the reaction centre in the transition state should be reflected by a change in magnitude of the β-effect (45), (54), (63).

Bartell (64), (65) has invoked nonbonded repulsion or steric hindrance as the chief cause of secondary isotope effects. According to him, there would be more and stronger nonbonded repulsions in the tetrahedral reactant than in the carbonium ion, considered to be a model for the transition state. To quantitatively formulate his postulate, his basic principle was that the amplitude of vibration of the hydrogen

atom was greater than that of the deuterium by a predictable amount. For a given nonbonded interaction, the isotope effect would be proportional to the mean square of the mass-sensitive component of the relative amplitude of vibration and to the second derivative of the potential function. Another assumption was that the nonbonded interaction between a hydrogen atom and any given atom may be approximated by a potential function, V, which is dependent on the distance r, between atoms, but independent of the orientation or deformation of the remainder of the molecule to which the atoms are attached. Using his formulation, he was able to calculate an isotope effect for the solvolysis of t-butyl chloride and this was approximately half of that observed for t-amyl chloride. Thus, at least qualitatively, nonbonded interactions contribute to the isotope effects.

However, Shiner (49) has pointed out that the isotope effect on the solvolysis of t-amyl chloride is approximately the same as on the solvolysis of t-butyl chloride. Bartell's calculations seemed to have overestimated the isotope effect by assuming a carbonium ion transition state. Halevi (44) also has criticised the simplifying assumptions made by Bartell. Thus, in the case of β-secondary isotope effects on the rates of solvolytic reactions, controversy hinges on the relative importance of hyperconjugation and the release of non-bonded interactions in producing the assumed reduction of a β C-H force constant in the activation process. The conformational dependence of such β-isotope effects and their transmission through unsaturated bonds have been explained by hyperconjugation by Shiner et al. However, steric interaction has not been overlooked (66).

In order to investigate the magnitude of secondary steric isotope effects in solvolytic reactions, a system should be found such that (a) hyperconjugation involving the isotopically substituted bond is prohibited and (b) release of nonbonded interactions in the vicinity of isotopic substitution plays a role in the activation process. Karabatsos et. al. (67) studied the solvolysis of 8-methyl- and 8-deuteromethyl-1-chloromethylnaphthalene. They observed a very small normal isotope effect and using Bartell's equations (65), they concluded that less than 10% of the observed β-secondary isotope effect in the solvolysis of simple tertiary alkyl halides can be attributed to release of steric strain.

More recently, Jewett and Dunlap (68) have found that the δ-deuterated analog of dimethylneopentylcarbinyl chloride $[(CR_3)_3CCH_2C(CH_3)_2Cl;\ R=H,\ D]$ reacts slightly faster than the non-deuterated compound in aqueous alcohol. But in the case of the allylic and acetylenic derivatives of the compound, where hyperconjugation with the electron-deficient solvolytic center is stereo-electronically possible, a normal δ-effect was observed. On the basis of this observation, they concluded that nonbonded interactions of the magnitude involved in usual solvolytic systems has a negligible effect on β C-H force constants and that a hyperconjugation model best explains β-secondary isotope effects on solvolytic reactions. These results are given in Table VI.

Streitwieser et. al. (70) observed that a change in hybridisation of a C-H or C-D bond in going to the transition state is often accompanied by a change in force constant for a vibration with a consequent isotope effect on the rate. An early example was found in the solvolysis of

TABLE VI (68)

δ-SECONDARY DEUTERIUM ISOTOPE EFFECTS

Compound		Solvent	k x 10^4 sec^{-1}	k_H/k_D
$(CR_3)_3CCH_2C(CH_3)_2Cl$;	R=H	80% EtOH	2.106 ± 0.002	0.983
	R=D		2.143 ± 0.002	
trans $CR_3CH=CHCHClCH_3$				
	R=H*		2.172 ± 0.001	
	R=D		1.919 ± 0.001	1.132
$CR_3C\equiv C-C(CH_3)_2Cl$		95% EtOH		1.095

*Refer (69)

cyclopentyl-1-d p-toluene sulfonate in acetic acid, for which k_H/k_D = 1.15 at 50°C (57), (70). The reaction involves an intermediate of the carbonium ion type. The experimental effect was interpreted as a change from a tetrahedral C-H bending vibration of the ground state to an out-of-plane bending motion of the transition state, which has the character of a nearly planar trigonal carbonium ion. The illustration in Figure 2 shows that

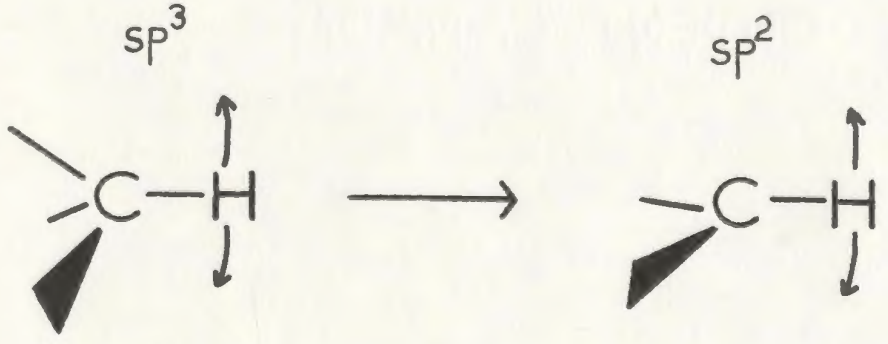


FIGURE 2.

the vibration is freer in the trigonal compound, thus it occurs at lower frequencies and has a lower zero-point energy. The heavier deuterium atom benefits less from this lower vibration and hence the deuterium compound solvolyzes at a lower rate. More recent evidence for this view has come from Belanić-Lipovac, Borčić and Sunko (71) who investigated the rate of solvolysis of 1,1 dimethyl-allyl-3,3-d_2 chloride [$(CH_3)_2CClCH{=}CD_2$ (IV)] and 3,3-dimethylallyl-1,1-d_2 chloride [$(CH_3)_2C{=}CHCD_2Cl$ (V)]. There was no appreciable isotope effect for the latter (V) but k_H/k_D for the former (IV) was found to be 1.2. It was pointed out that in (IV), the C-D bonding orbitals are already sp^2 hybridised in the ground state, and assuming that with respect to the positive charge the transition state in both the above mentioned chlorides is similar, this would mean that no rehybridisation would occur in the solvolysis of (IV). Since the C-D bonding orbitals in (V) are orthogonal to the π-system in the transition state, a rate retardation due to hyperconjugation would not be observable. However, it was felt that there might be an inverse isotope effect for (V). One of the reasons was, that the electron withdrawing substituents had been found to increase the C-H out-of-plane bending frequency in ethylene. Therefore, the electron demand on the double bond in the form of stabilisation of the transition state by allylic resonance should have resulted in stiffening of the C-D bonds and a subsequent rate acceleration. An inverse effect might also have been expected due to the fact that deuterium has a larger electron releasing power than hydrogen.

Halevi et. al. had a somewhat different approach. They felt

that in addition to the gross effect of a change in mass on the vibrational frequencies, there might be more subtle influences that would lead to appreciable differences in ground state properties such as electron distribution or resonance energy, and as a result of which a CD_3 group for example could be regarded as a different substituent from an ordinary methyl group. They have focussed attention on the fact that mean lengths of bonds to hydrogen and deuterium are different (72). This arises as a consequence of the effect of a lower ground-state potential energy for the deuterium containing molecule, connected with the asymmetry of the potential surface describing the energy of the molecule with respect to the displacement of the atoms in bond-stretching and bond-shortening directions. Since the potential surface rises more steeply for bond-shortening, the mean positions of atoms for a molecule in a given vibrational state will correspond to increasing bond distances as the energy of the state increases, so that the lower potential energy deuterium compound will have effectively shorter bonds than the protium compound. Due to the altered bond length, dipolar and other interactions will be altered and the behaviour of C-H bonds and C-D bonds w.r.t. inductive and hyperconjugative effects will be different, quite apart from the consequences of altered vibrations produced by the activation process. [Weston (73) has criticised this view by showing that isotopic perturbation of the potential energy hypersurface is negligible.] From experiment, deuterium bonded to carbon appears to be more electropositive (74), (75) but less polarizable (80) than protium. Halevi et. al. too,

from experiment (76), (77), (78), (79) deduced that hyperconjugative electron release is reduced in the CD_3 group, compared with the CH_3 group. It might therefore be expected that of the 2 isotopes, a deuterium located at the reaction site (α-effect) or adjacent to it (β-effect) will be more effective in stabilising the positive charge which develops in the transition state of most solvolytic processes and will give an isotope effect which is less than one. Usually, however, isotope effects are greater than one and this makes it difficult to assess experimentally the contribution of the inductive effect to secondary isotope effects. Halevi (44) has attempted to calculate the inductive isotope effect and has been able to qualitatively reconcile it with shifts in vibrational frequencies. However, he admits that with his model the actual calculation of these shifts and the corresponding isotope effect cannot be carried out in any real case.

Work supporting the inductive isotope effect has come from Streitwieser et. al. (81), (82) who have attempted to ascertain the extent to which deuterium acts as a normal electron donating substituent, by determining the effect of deuteration on the pK_a's of several carboxylic acids. The results of Streitwieser's study indicate that deuteration lowers acidity of the acid. K_H/K_D for $(CD_3)CH_3COOH = 1.032 \pm 0.002$, a result which would be predicted by an inductive effect of D. Similar observations were made by Nussim and Ron (83). The systems, they studied, were as different as acetic acid-d_3 vs acetic acid on the one hand and 2 , 4 , 6-trinitro-N-methylaniline on the other; the acid dissociation constant was 10 - 12% lower and the basic dissociation constant correspondingly

higher in the deuterated compound. Moreover, the constancy of the effect per α-deuterium atom and its strong damping through a saturated carbon atom were suggestive of the fact that inductive electron release from CD_3 or CD_2 was greater than from CH_3 or CH_2 respectively.

From the foregoing discussions, it appears that the origin of the secondary deuterium isotope effect cannot be attributed solely to either steric, hyperconjugative or inductive effects. Rather, if the rationales that have been presented are the only ones possible, it appears that many secondary isotope effects have more than one influence acting on them, this being a function of the system being investigated. The main difficulty in interpreting these effects appears to lie in differentiating and evaluating the various factors which influence the magnitude of the overall effect.

In the present study on the secondary deuterium isotope effects of trifluoroacetates, deuterated in the alkyl part, explanation of the results will be based on the above discussion.

EXPERIMENTAL

I. PREPARATION OF MATERIALS

All the esters examined in this work were synthesized as recorded below:

(a) Methyl trifluoroacetate ($CF_3COOOCH_3$)

$$CF_3COOAg + CH_3I \xrightarrow[\text{Solvent}]{C_6H_5CN} CF_3COOCH_3 + AgI\downarrow$$

CH_3I (Fisher Scientific Co.) was purified by washing with dilute sodium thiosulphate first and subsequently with water. The iodide was dried over anhydrous calcium chloride and distilled. It boiled at 42.3°C and was carefully preserved in the dark.

Benzonitrile (Eastman Organic Chemicals) was purified by drying preliminarily over anhydrous magnesium sulphate and then distilling from over phosphorous pentoxide.

Silver trifluoroacetate (0.07 mole) (Eastman Organic Chemicals) was dissolved in freshly distilled benzonitrile (50 ml.). Purified methyl idodide (0.05 mole) in benzonitrile (25 ml.) was added to the reaction vessel, over a period of twenty minutes. The reaction proceeded at room temperature for twenty-four hours, at the end of which, the product was isolated by distillation. Its boiling range was 42 - 43°C. The ester was redistilled. The NMR spectrum of the ester indicated complete absence of CH_3I.

B.P. = 43°C. The yield obtained from repeated preparations was between 58% to 70%.

(b) Methyl-d_3-trifluoroacetate (CF_3COOCD_3)

This was prepared in a similar manner to CF_3COOCH_3 using methyl-d_3-iodide (Merck, Sharp, Dohme Ltd.). Mass spectral evidence indicated the complete absence of CD_3I.

B.P. = 43°C. Yields varied between 50% and 70%.

(c) Ethyl trifluoroacetate ($CF_3COOCH_2CH_3$)

Ethyl bromide (Eastman Organic Chemicals) was used for the preparation which was similar to (a).

B.P. = 59°C. The yield varied between 50% and 70%.

(d) Ethyl-d_5-trifluoroacetate ($CF_3COOCD_2CD_3$)

Ethyl-d_5-bromide (Merck, Sharp, Dohme Ltd.) was utilised for the preparation which was similar to that of (a).

B. P. = 59.2°C - 60°C. Yields varied between 50% and 70%.

(e) Isopropyl trifluoroacetate ($CF_3COOCH(CH_3)_2$)

This was synthesized by a method used by Bourne et. al. (84)

$$(CF_3CO)_2O + (CH_3)_2CHOH \xrightarrow{CF_3COOAg} CF_3COOCH(CH_3)_2 + CF_3COOH.$$

Isopropyl alcohol (Fisher Scientific Company) was purified before use, by reaction with magnesium.

Isopropyl alcohol (0.068 mole) was gently added to the reaction vessel containing trifluoroacetic anhydride (1.3 moles) and

silver trifluoroacetate (0.2 gms.), over an interval of five minutes. After the initial vigour of the reaction had subsided, the mixture was gently refluxed for fifteen minutes. Ice-water was then added to the mixture and it was neutralized with cold 2N NaOH to pH 7-8. The organic phase was then completely separated, dried over anhydrous magnesium sulphate and distilled.

The fraction distilling between 72°C and 73°C was retained. Yields varied from 48% to 75%.

(f) Isopropyl-d_6-trifluoroacetate ($CF_3COOCH(CD_3)_2$)

Isopropyl-d_6-alcohol had to be synthesized for the preparation of the ester. It was prepared from acetone-d_6 (Merck, Sharp, Dohme Ltd.) by Shiner's method (85).

$$4\ (CD_3)_2CO + LiAlH_4 \longrightarrow [(CD_3)_2CHO]_4LiAl$$

$$[(CD_3)_2CHO]_4LiAl + 4ROH \longrightarrow 4(CD_3)_2CHOH + LiAl(OR)_4$$

where ROH is $CH_3CH_2CH_2CH_2OCH_2CH_2OCH_2CH_2OH$ i.e. n-butyl carbitol. This reagent and diethyl carbitol in place of diethyl ether, had been initially used by Nystrom, Yanko and Brown (86), for the reduction of carbon dioxide to methanol, using lithium aluminium hydride as reducing agent. The use of the carbitols is very convenient as it eliminates the use of water and the subsequent separation of the alcohol from water.

The solvents used were purified as follows: (i) Diethyl carbitol (Matheson, Coleman and Bell Ltd.) was dried over anhydrous

magnesium sulphate, then calcium hydride and distilled at reduced pressure from $LiAlH_4$.

B.P. = 86°C at 10 mm.

(ii) n-Butyl carbitol (Matheson, Coleman and Bell Ltd.) was dried over anhydrous potassium carbonate, filtered and fractionally distilled at reduced pressure.

B.P. = 70°C at 0.3 mm.

Lithium aluminium hydride (0.075 mole) (Alpha Inorganics Inc.) in diethyl carbitol (50 ml.) was stirred in a 3-necked flask fitted with a double-jacketed condenser, a mechanical stirrer and dropping funnel. Purified spectrograde acetone (0.173 mole) (Fisher Scientific Co.) in diethyl carbitol (25 ml.) was added through a dropping funnel to the reaction vessel, over a period of one hour. The reaction vessel was placed in an ice-trough to prevent the acetone from volatilising. The reaction mixture was stirred for approximately ten hours, after which n-butyl carbitol (85 ml.) was added slowly, over a period of one hour. The mixture was kept stirred overnight, in order to decompose the alcoholate and destroy the excess $LiAlH_4$. The product was isolated by distillation. The crude product was redistilled.

B. P. = 82.3°C. Yield ca. 90%.

The alcohol obtained was checked for purity by nuclear magnetic resonance, infrared spectrometry and gas liquid chromatography. The infrared spectrum showed complete absence of C = O, indicating the total reduction of acetone by $LiAlH_4$. Using Apiezon and

QF 1 columns in the GLC, no acetone was detected. The NMR spectrum too, indicated the complete absence of acetone.

Isopropyl-d_6-alcohol, obtained above, was used to prepare the ester in a similar manner to (e).

B. P. = 73°C and yield = 48%.

(g) Tertiary butyl trifluoroacetate [$CF_3COOC(CH_3)_3$]

Tertiary butyl alcohol (Fisher Scientific Co.) was purified by fractional freezing and used for the preparation of the ester by method (e).

B. P. = 84°C. Yield = 45%.

(h) Tertiary butyl-d_9-trifluoroacetate [$CF_3COOC(CD_3)_3$]

This was prepared by method (e) from tertiary butyl-d_9-alcohol (Merck, Sharp, Dohme Ltd.).

B. P. = 85°C. Yield = 47%.

From a comparison of NMR spectra, we showed that $CF_3COOC(CD_3)_3$ contained the same concentration of deuterium, as was in the tertiary butyl-d_9-alcohol, i.e. 99%.

The physical properties of the eight esters are recorded in Table VII.

TABLE VII

SOME PHYSICAL PROPERTIES OF ESTERS DERIVED FROM TRIFLUOROACETIC ACID

Ester	B.P. °C 760 mm	NMR* τ
CF_3COOCH_3	43 (43)	6.04 (6.02)
CF_3COOCD_3	42.5-43	-
$CF_3COOCH_2CH_3$	59 (61.3)	8.68, 5.60 (8.58, 5.54)
$CF_3COOCD_2CD_3$	59.2-60	-
$CF_3COOCH(CH_3)_2$	72.5-73 (73)	8.66, 4.81 (8.64, 4.83)
$CF_3COOCH(CD_3)_2$	73	4.85
$CF_3COOC(CH_3)_3$	84	8.45
$CF_3COOC(CD_3)_3$	85 (45°C at 145 mm)	-

*NMR spectra were recorded on a Varian A-60 spectrometer and peaks were recorded on the τ scale relative to tetramethylsilane as an internal reference.

Values in parentheses are literature values.

II. PREPARATION OF SOLUTIONS

Conductivity Water: was obtained by passing tap water through AR-grade Amberlite MB-1 into a Barnsted still. A distillate of 0.001 ppm total solid content, with electrical resistances varying from 1.5 to 5 million ohms per ml. is obtainable from the still. The distilled water was stored in a three-necked ten-litre round-bottomed flask, fitted with Teflon stoppers. The distillate was passed through another cylinder containing amberlite in order to remove carbon-dioxide dissolved in the water after distillation, prior to the preparation of ester solution.

Backing electrolyte: was prepared for the kinetics of certain esters in order to lower the initial resistances to those measurable on the conductivity bridge. The appropriate substrate (ca. 3 µl) in 1000 ml. of conductivity water was allowed to stand overnight so that hydrolysis of the ester takes place and the resistance of the water to be used in the cells is lowered to 10,000 - 30,000 ohms.

The solution to be used in the cell was prepared as follows: Water (25 ml) from the purification train (see above) was placed in a 50 ml. stoppered flask, which was placed in the constant temperature bath. The cell was filled with backing electrolyte and 1 ml of solution withdrawn from it. It was also placed in the bath and left for half an hour, in order to reach thermal equilibrium. The ester (3 µl) i.e. enough to produce a 10^{-5} M to 10^{-4} M solution, was added to the distilled water (25 ml.) in the flask and shaken for at least 60 - 80 seconds. One ml. of this solution was then added to the backing electrolyte in the cell

and the cell was stirred for five to ten minutes to homogenize the solution before resistances were measured. This step was essential, as the esters were not easily soluble in water and this often led to supersaturation.

III. DESCRIPTION OF APPARATUS

(a) Constant Temperature Bath

The bath (see Figs. 3 and 4) consists of a 39" x 29" x 24" metal-framed unit, which supports a stainless steel tank of dimensions 28" x 13" x 18", surrounded by a 1" coating of styrofoam on the outside; this serving as the constant temperature water bath. Below this is another insulated stainless steel tank containing approximately 30% glycol solution, which is cooled by a Tecumseh ¼ h.p. refrigerator. Cooling coils made of ca. 25 ft. of copper tubing wound in five spirals placed ca. 2" apart are at the bottom of the water bath. The cooled glycol from the lower bath is pumped by a circulating pump, through rubber tubing. The rate of flow of the cold glycol is manipulated by a by-pass arrangement using two valves. The temperature of the glycol bath is monitored by a Fenwal Electronics thermistor (LB21J1) in a Wheatstone bridge circuit. Usually, the temperature gradient between the glycol bath and the water bath was kept at 5°C to give the best possible temperature regulation of the water bath. The simultaneous use of a cooling system and a heating arrangement is essential in the present study, in order to obtain a constant temperature, within ± 0.005°C.

The heat to the water bath was supplied via a Sargent

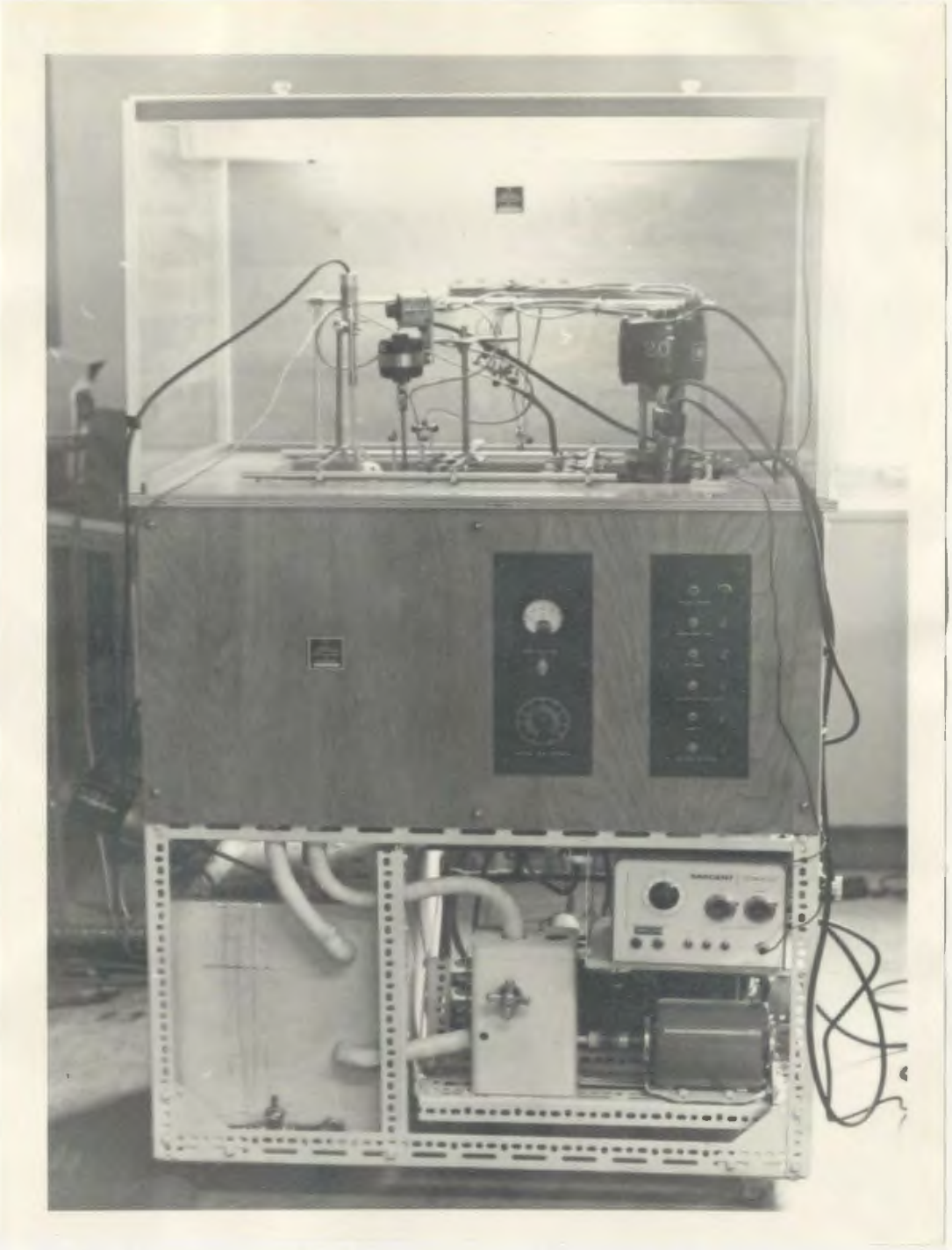


FIGURE 3. THERMOSTAT

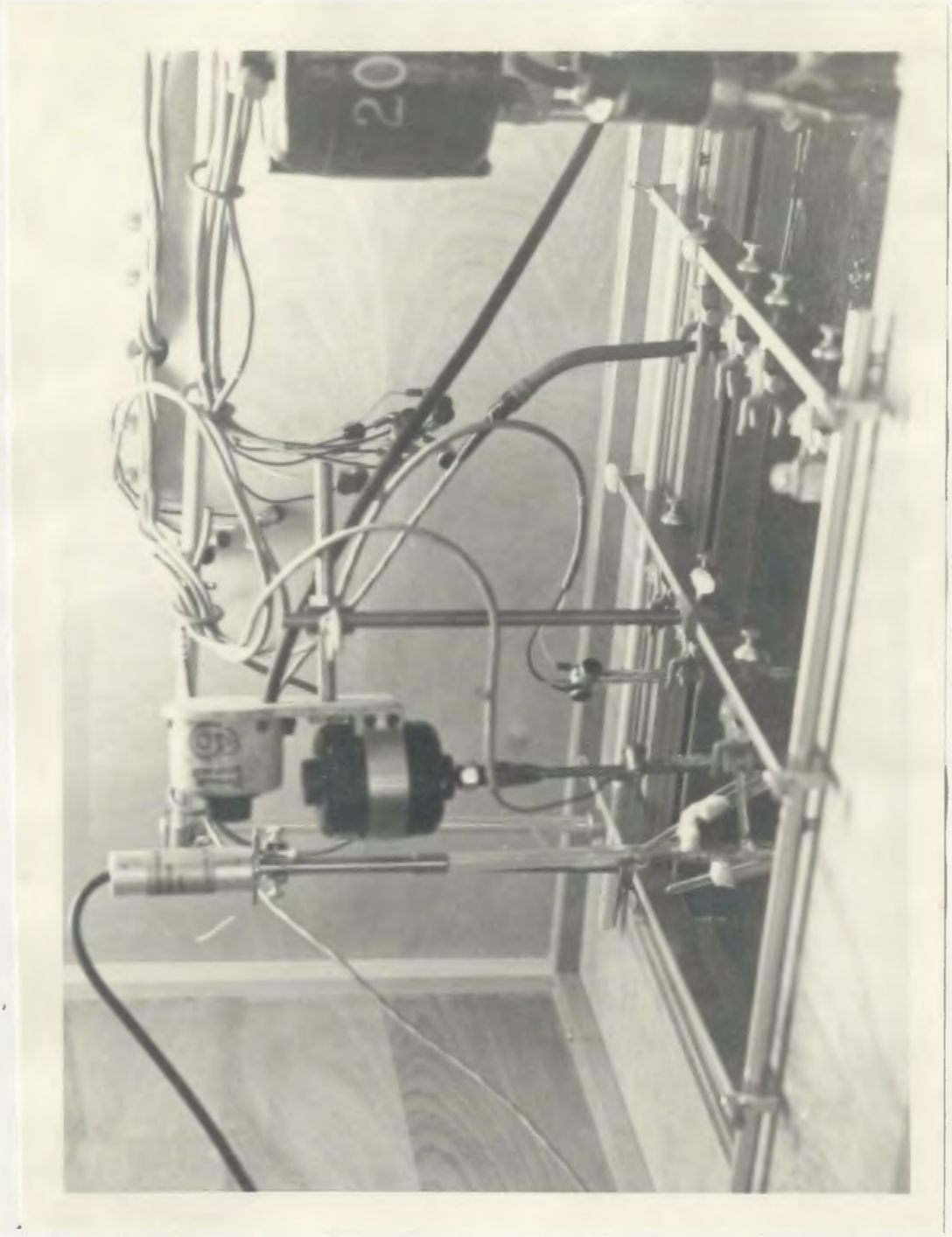


FIGURE 4. CLOSE-UP OF THERMOSTAT BATH

"Thermonitor" (S-82050) which had been modified slightly for better performance, by changing the voltage across the Thermistor-Wheatstone bridge from 6 to 4 volts. The Sargent "Thermonitor" consisted of a background heater (250 watts) which was controlled by a Variac on the control box and an intermittent knife-heater (250 watts), controlled by a Thermistor-Wheatstone bridge circuit coupled to a variable reactor.

During the latter part of the study, the Sargent "Thermonitor" was replaced by the Tronac "PTC-1000 A" which gave a temperature control to a precision of ± 0.002°C. Control was accomplished with a type one servo system, and on the whole, it was found to give better regulation than the Sargent "Thermonitor".

The water in the upper bath was kept stirred constantly by a Cenco Centrifugal Electric stirrer (circulating capacity, 105 gallons of water per minute) mounted in one corner of the bath. The cooled glycol from the lower bath and the heat supplied by the "Thermonitor" (or PTC-1000A) to the water, maintained the constancy of the temperature, with the aid of the powerful stirrer. The room, in which the bath was placed, was airconditioned, which prevented any appreciable change in temperature in the room from influencing the constant temperature of the bath.

(b) Conductivity Bridge

This is essentially a General Radio Impedance Comparator, type 1605-A and measures on meters, the magnitude and phase-angle differences between two external impedances.

This GRI Comparator is a self-contained system and consists of a signal source, a bridge and a detecting circuit. The bridge proper consists of the two external impedances to be compared and two very precise unity ratio arms. The ratio arms being equal to within one part in 10^6, the accuracy of impedance measurement depends largely on the precision of the external standard. The combination of four decade frequencies from 100 cps to 100 Kcps with a very wide impedance range and several difference ranges, gives the instrument flexibility.

Description of the oscillator, amplifier and bridge circuit is given in the General Radio operating instructions for an Impedance Comparator, type 1605-A.

Standard Impedance. A General Radio resistance box, type 1432, is used as a standard with a range of 0.1 ohms to 111,111 ohms. The accuracy of the resistance increments is given as ± 0.05%.

(c) Thermometry

A Tinsley Platinum Resistance Thermometer calibrated by the National Physical Laboratory, Teddington, England, was used in conjunction with a Mueller Temperature Bridge, type 4772 (manufactured by Tinsley and Company). It was found necessary to check the ice-point of the thermometer and the ratio-arm of the bridge, before regulation of the bath at each new temperature, because the resistance of the thermometer at zero degrees centigrade, changed from time to time. The ice-point was measured as follows: ice obtained from a "Scotsman" ice-machine was taken in a two-litre Dewar. Conductivity water was added to it and a

slurry of ice in water was obtained by agitating the mixture with a glass rod. The water was drained off and more conductivity water added to the ice to prepare a slush. The Platinum Resistance Thermometer was placed in it, such that proper contact of the former with the ice-water mixture was ensured. Some time was allowed for the thermometer to equilibrate with the ice-water slush. Resistance readings were then taken at regular intervals, until there was no apparent change in consecutive readings. The ice point, R_o, measured by N. P. L., was 24.923 ohms. The ice-point determined during the present study varied between 24.9270 and 24.9276 ohms. The new R_o values were used for the temperature determinations.

The balance-point, for measurement of temperatures with the help of the Platinum Resistance Thermometer, was determined by a D-C Null Detector, manufactured by Leeds and Northrup. A Honeywell recorder was used to observe the fluctuations in bath temperature, during a kinetic run and while changing the bath temperature. A Fenwal thermistor served as one arm in a Wheatstone bridge circuit and fine resistors were used to control the sensitivity of the recorder. The chart-paper, used for the recorder, was calibrated with the help of a Beckmann thermometer.

(d) Conductivity Cells

The cells (see Fig. 5) used were similar to those used by Hyne and Robertson (87). Through the middle of the cells ran a rotating shaft, on top of which was a small glass enclosed magnet, which could keep the solution in the cell stirred, by using an external magnetic stirrer, the speed of which was controlled by means of a Variac. The

FIGURE 5. CONDUCTANCE CELL

cells were "conditioned" to the particular ester before the kinetic run was carried out with it, by filling them with backing electrolyte and carrying out several experiments till the rates measured agreed within ± 0.3% at the same temperature.

IV. GUGGENHEIM-ROBERTSON METHOD

The rates of solvolyses of the esters were determined by a precise conductimetric method, based on the Guggenheim treatment (88) in a form elaborated by Robertson (89). The Guggenheim-Robertson Method (GRM) has been found excellent for determining solvolytic rates in pure water in cases where the acid related to the leaving group is strong (89). However, trifluoroacetic acid is a weak acid, with pKa = 0.23 at 25°C (90). The validity of the method for use in the present study i.e., where the acid related to the leaving group is weak, has been discussed in detail by Winter (1).

Ives (91) has suggested that the classical Ostwald Dilution Law, stated in terms of conductance parameters in a form, which neglects the effect of ionic strength on both the activity and mobility of the weak electrolyte, accurately represents the variation of the equivalent conductance of the weak electrolyte as a function of concentration at high dilution ($< 10^{-4}$ M). In relation to the present work, Ives' suggestion means that the variation of the equivalent conductance (Λ) of the weak electrolyte with concentration (C) is accurately represented by

equation:

$$\frac{1}{\Lambda} = \frac{1}{\Lambda_o} + \frac{\Lambda C}{K_c \Lambda_o^2} \qquad (1)$$

where

Λ = equivalent conductance of the weak electrolyte of concentration 'C'.

Λ_o = limiting equivalent conductance

K_c = classical dissociation constant, not corrected for the variation of activities or mobilities with ionic strength. The equivalent conductance Λ is related to the experimental parameters by the equation:

$$\Lambda = \frac{10^3 \kappa}{RC} \qquad (2)$$

where,

κ = cell constant

R = resistance of the solution in ohms, and

C = concentration of the solution in moles/litre.

Combining equations (1) and (2)

$$\frac{RC}{\kappa 10^3} = \frac{1}{\Lambda_o} + \frac{\kappa 10^3}{K_c \Lambda_o^2 R} \qquad (3)$$

$$C = \frac{\kappa 10^3}{\Lambda_o} \cdot \frac{1}{R} + \frac{\kappa^2 10^6}{\Lambda_o^2 K_c R^2} \qquad (4)$$

Defining a constant $P = \frac{10^3 \kappa}{\Lambda_o}$ we get

$$C = \frac{P}{R} + \frac{P^2}{K_c R^2} \qquad (5)$$

At a fixed temperature, P will be a constant for a given electrolyte and reaction vessel (cell). Equation (5) shows that the simple relationship between the concentration of the acid and the reciprocal of the resistance used by Robertson (89) for strong acids, is modified in the case of a weak acid by a second term $\frac{P^2}{K_c R^2}$. For a pseudo first order reaction, the rate equation is the following:

$$C_t = C_o e^{-kt} \qquad (6)$$

where,

C_o = initial concentration of substrate, and

C_t = concentration of substrate at time t.

Hence, in order to know k, C_o must be known and generally speaking it is not very easy to measure the quantity accurately. The first order rate constant can be obtained from a plot of $\log C_t$ vs. t, provided C_o is known.

The GRM avoids the difficulty of determining C_o. The Guggenheim equation (5) for the evaluation of the pseudo first order rate constant in a solvolysis reaction is

$$C_{t+\tau} - C_t = C_o e^{-kt} \cdot (1 - e^{-k\tau}) \qquad (7)$$

where,

C_o = initial concentration of substrate (ester in this case)

C_t = concentration of the product (acid) at time t

$C_{t+\tau}$ = concentration at time $t+\tau$

k = pseudo first order rate constant

τ = arbitrary time interval between two sets of observations

required in a Guggenheim first order rate constant determination, greater than twice the half-life of a reaction.

In this method, measurements of concentrations are taken at times t_1, t_2, t_3, ... t_n, and $t_{1+\tau}$, $t_{2+\tau}$, $t_{3+\tau}$, ... $t_{n+\tau}$, where τ is the interval between two sets of readings, greater than two half-lives (see Fig. 6).

Substituting equation (5) into equation (7) gives the following:

$$\left[\frac{P}{R_{t+\tau}} + \frac{P^2}{K_c R^2_{t+\tau}}\right] - \left[\frac{P}{R_t} + \frac{P^2}{K_c R_t^2}\right] = C_o e^{-kt} \cdot (1-e^{-k\tau})$$

$$\therefore P\left[\frac{1}{R_{t+\tau}} - \frac{1}{R_t}\right] + \frac{P^2}{K_c}\left[\frac{1}{R^2_{t+\tau}} - \frac{1}{R^2_t}\right] = C_o e^{-kt} \cdot (1-e^{-k\tau})$$

$$\therefore P\left[\frac{1}{R_{t+\tau}} - \frac{1}{R_t}\right]\left[1 + \frac{P}{K_c}\left(\frac{1}{R_{t+\tau}} + \frac{1}{R_t}\right)\right] = C_o \cdot (1-e^{-k\tau}) \cdot e^{-kt} \qquad (8)$$

$$\therefore \left[\frac{1}{R_{t+\tau}} - \frac{1}{R_t}\right]\left[1 + \frac{P}{K_c}\left(\frac{1}{R_{t+\tau}} + \frac{1}{R_t}\right)\right] = \frac{C_o(1-e^{-k\tau})\ e^{-kt}}{P} \qquad (9)$$

For a given experiment, the factor $\frac{C_o(1-e^{-kt})}{P}$ is a constant, Q, say

$$\therefore \left[\frac{1}{R_{t+\tau}} - \frac{1}{R_t}\right]\left[1 + \frac{P}{K_c}\left(\frac{1}{R_{t+\tau}} + \frac{1}{R_t}\right)\right] = Qe^{-kt} \qquad (10)$$

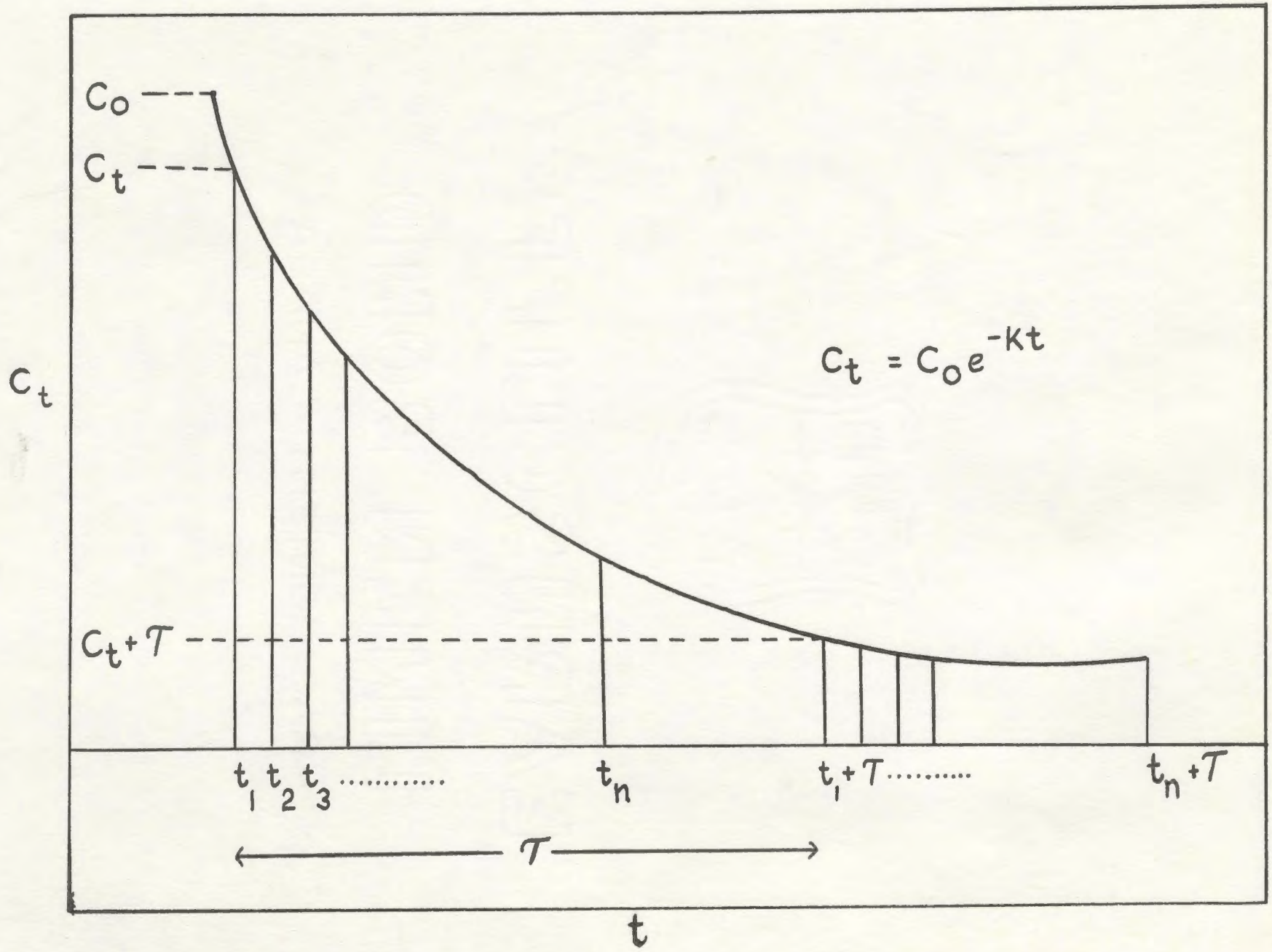


FIGURE 6. SCHEMATIC ILLUSTRATION OF THE GUGGENHEIM METHOD.

Taking logs of both sides, the expression obtained is:

$$\log\left[\frac{1}{R_{t+\tau}} - \frac{1}{R_t}\right] + \log\left[1 + \frac{P}{K_c}\left(\frac{1}{R_{t+\tau}} + \frac{1}{R_t}\right)\right] = \log Q - \frac{kt}{2.3026} \qquad (11)$$

From equation (11) it is obvious that a plot of $\log\left[\frac{1}{R_{t+\tau}} - \frac{1}{R_t}\right]$ versus time will be linear, of slope = $\frac{k}{2.3026}$, only if

$\frac{P}{K_c}\left(\frac{1}{R_{t+\tau}} + \frac{1}{R_t}\right)$ is negligible. If, Λ_o and K_c for the weak acid are known, it is possible to calculate the magnitude of the term and hence estimate its importance in equation (11). A calculation of this sort was done by Winter and Scott (29) and the effect of the term $\frac{P}{K_c}\left(\frac{1}{R_{t+\tau}} + \frac{1}{R_t}\right)$ was found to be very small and well outside the limits of reproducibility offered by the GRM (33).

A further requirement, of any precise determination of a rate constant, is that the parameter should be constant over the complete reaction. Since the hydrolyses of trifluoroacetates are known to be acid catalysed (23), (92), (93), it was important to demonstrate that no autocatalysis occurred with the present systems. The GRM requires at least three half-lives for the determination of a rate constant since the parameters $R_{t+\tau}$ and R_t are each observed over the period of one half-life ($t_{\frac{1}{2}}$) and ideally the interval between the two sets of observations should satisfy the condition $t > 2t_{\frac{1}{2}}$. This means, that the rate constants as usually determined represent at least 87.5% of a complete reaction. By deliberately extending (1) the measurement of the resistances of a reacting solution over four separate half-lives and observing the resistances at identical time intervals, three rate con-

stants were obtained, one of which covered at least 93.3% of the reaction. The rates obtained from the four sets were well within the limit of reproducibility offered by the GRM. This particular experiment confirmed that there was no perceptible acid catalysis in these reactions and that the linear relationship between the conductance and the concentration of the product (acid) is valid over the range of substrate concentrations used.

V. RATE CONSTANTS

The rate constants, which have been measured for the methyl, ethyl, isopropyl and tertiary butyl trifluoroacetates, both non-deuterated and deuterated, in water, are reported in Tables VIII and IX, along with calculated rates and deviations. At each temperature at least four rate determinations were carried out and the reproducibility in any given set of runs, at any temperature, was within ± 0.5%. Several runs had to be eliminated because of supersaturation, due to the low solubility of the esters in water. Such supersaturated runs gave curvilinear plots instead of just linear plots. These runs have not been included in the calculations. In each of the runs, the rates were calculated from the plots done on a large scale graph paper and from linear least squares computed on the Programma 101 (Olivetti Underwood). Tables show rates, which have been computed from linear least squares.

The temperature dependence of the rates of hydrolysis of the methyl, ethyl, isopropyl esters could be represented adequately by the equation:

$$\log (k/T) = \frac{A}{B} + B$$

for both deuterated and non-deuterated esters. The values of A and B were determined by least squares and the thermodynamic parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were calculated from the Eyring equation which gives

$$A = - \frac{\Delta H^{\ddagger}}{2.3026R} \tag{13}$$

$$B = \frac{\Delta S^{\ddagger}}{2.3026R} + \log (k/h) \tag{14}$$

The values of the thermodynamic parameters for the esters are given in Table X and the values of A and B obtained by least squares are reported in Table XI. Table XII reports average rates of non-deuterated and deuterated esters at 5°C, 10°C, 15°C and 25°C (the last temperature is applicable only to t-butyl trifluoroacetate). In Table XIII are reported the isotope effects for the four esters at the above mentioned temperatures.

TABLE VIII

RATES OF SOLVOLYSIS OF NON-DEUTERATED TRIFLUOROACETATES IN WATER

Ester	Temperature ^{o}K	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
CF_3COOCH_3	278.124	23.52	23.44	+ 0.08
	278.124	23.45	23.44	+ 0.01
	278.130	23.52	23.45	+ 0.07
	278.111	23.52	23.42	+ 0.10
	278.109	23.47	23.42	+ 0.05
	278.112	23.37	23.42	- 0.05
	278.128	23.47	23.45	+ 0.02
	278.125	23.38	23.44	- 0.06
	278.116	23.40	23.43	+ 0.03
	278.116	23.39	23.43	- 0.04
	278.118	23.37	23.43	- 0.06
	278.117	23.42	23.43	+ 0.01
	278.128	23.38	23.45	- 0.07
	278.128	23.36	23.45	- 0.09
	278.126	23.35	23.45	- 0.09
	278.127	23.37	23.45	- 0.08
	283.168	33.50	33.32	+ 0.18
	283.166	33.48	33.31	+ 0.17
	283.168	33.43	33.32	+ 0.09

TABLE VIII (Continued)

Ester	Temperature ^{o}K	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
	283.168	33.36	33.32	+ 0.04
	283.168	33.49	33.32	+ 0.17
	288.162	46.51	46.63	- 0.12
	288.161	46.51	46.63	- 0.12
	288.162	46.51	46.63	- 0.12
	288.162	46.51	46.63	- 0.12
$CF_3COOCH_2CH_3$	278.162	8.869	8.855	+ 0.014
	278.162	8.813	8.855	- 0.042
	278.161	8.858	8.855	+ 0.003
	278.161	8.809	8.855	- 0.046
	278.160	8.849	8.854	- 0.005
	278.160	8.809	8.854	- 0.046
	278.162	8.847	8.855	- 0.008
	278.162	8.840	8.855	- 0.015
	283.165	12.68	12.62	+ 0.06
	283.165	12.67	12.62	+ 0.05
	283.160	12.66	12.62	+ 0.04
	283.160	12.68	12.62	+ 0.06
	283.161	12.72	12.62	+ 0.10
	283.161	12.74	12.62	+ 0.12

TABLE VIII (Continued)

Ester	Temperature $^{\circ}K$	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
	288.156	17.68	17.76	- 0.08
	288.160	17.70	17.77	- 0.07
	288.162	17.71	17.77	- 0.06
	288.160	17.68	17.77	- 0.09
$CF_3COOCH(CH_3)_2$	278.159	2.478	2.469	+ 0.008
	278.159	2.463	2.469	- 0.006
	278.159	2.445	2.469	- 0.024
	278.162	2.466	2.470	- 0.004
	278.162	2.477	2.470	+ 0.007
	278.162	2.452	2.470	- 0.018
	278.162	2.473	2.470	+ 0.003
	283.160	3.548	3.536	+ 0.012
	283.160	3.525	3.536	- 0.011
	283.160	3.522	3.536	- 0.014
	283.161	3.579	3.537	+ 0.042
	283.161	3.578	3.537	+ 0.041
	283.160	3.572	3.536	+ 0.036

TABLE VIII (Continued)

Ester	Temperature °K	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
	288.161	4.983	5.004	- 0.021
	288.161	5.002	5.004	- 0.002
	288.161	4.983	5.004	- 0.021
	288.161	4.958	5.004	- 0.046
	288.161	4.990	5.004	- 0.014
	288.161	5.017	5.004	+ 0.013
	288.160	5.018	5.004	+ 0.014
$CF_3COOC(CH_3)_3$	298.162	14.06	-	-
	298.161	14.08	-	-
	298.160	14.22	-	-
	298.160	14.00	-	-
	298.161	14.43	-	-
	298.161	13.82	-	-
	298.160	14.01	-	-

The minor differences in rate for the four protium esters reported here, when compared to those reported in (1), are considered insignificant. The new data is, however, to be preferred.

TABLE IX

RATES OF SOLVOLYSIS OF DEUTERATED TRIFLUOROACETATES IN WATER

Ester	Temperature ^{o}K	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
CF_3COOCD_3	278.124	22.31	22.34	- 0.03
	278.124	22.31	22.34	- 0.08
	278.124	22.31	22.34	- 0.03
	278.123	22.25	22.33	- 0.03
	283.167	31.78	31.65	+ 0.13
	283.166	31.72	31.65	+ 0.07
	283.166	31.72	31.65	+ 0.07
	283.166	31.78	31.65	+ 0.13
	283.166	31.71	31.65	+ 0.06
	288.162	44.12	44.19	- 0.07
	288.161	44.16	44.19	- 0.03
	288.160	44.09	44.18	- 0.09
	288.160	44.09	44.18	- 0.09
	288.159	44.19	44.18	+ 0.01
	288.159	44.12	44.18	- 0.06
$CF_3COOCD_2CD_3$	278.160	8.524	8.542	- 0.018
	278.160	8.538	8.542	- 0.004
	278.160	8.543	8.542	+ 0.001

TABLE IX (Continued)

Ester	Temperature ^oK	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
	278.161	8.529	8.542	- 0.013
	278.161	8.520	8.542	- 0.022
	278.161	8.533	8.542	- 0.009
	283.161	12.28	12.16	+ 0.12
	283.161	12.26	12.16	+ 0.10
	283.160	12.22	12.16	+ 0.06
	283.160	12.22	12.16	+ 0.06
	288.159	17.01	17.09	- 0.08
	288.159	17.06	17.09	- 0.03
	288.159	17.06	17.09	- 0.03
	288.160	17.07	17.09	- 0.02
	288.161	17.13	17.09	+ 0.04
$CF_3COOCH(CD_3)_2$	278.161	2.401	2.410	- 0.009
	278.161	2.395	2.410	- 0.015
	278.161	2.385	2.410	- 0.025
	278.161	2.427	2.410	+ 0.017
	278.161	2.418	2.410	+ 0.008
	278.161	2.384	2.410	- 0.026
	283.160	3.474	3.444	+ 0.030
	283.160	3.473	3.444	+ 0.029
	283.160	3.483	3.444	+ 0.039

TABLE IX (Continued)

Ester	Temperature ^oK	k_{exp} x $10^4 sec^{-1}$	k_{calc} x $10^4 sec^{-1}$	$k_{exp}-k_{calc}$ x $10^4 sec^{-1}$
	283.160	3.468	3.444	+ 0.024
	283.160	3.469	3.444	+ 0.025
	288.161	4.830	4.864	- 0.034
	288.161	4.832	4.864	- 0.032
	288.161	4.846	4.864	- 0.018
	288.161	4.847	4.864	- 0.017
	288.161	4.864	4.864	- 0.000
$CF_3COOC(CD_3)_3$	298.161	6.679	-	-
	298.161	6.599	-	-
	298.160	6.536	-	-
	298.160	6.244	-	-
	298.160	6.707	-	-
	298.160	6.503	-	-
	298.162	6.627	-	-
	298.162	6.330	-	-
	298.162	6.222	-	-
	298.162	6.510	-	-
	298.162	6.296	-	-

TABLE X

THERMODYNAMIC PARAMETERS (AT 10°C) FOR THE SOLVOLYSIS OF SOME DEUTERATED AND NON-DEUTERATED TRIFLUOROACETATES IN H_2O

CF_3COOR (-R)	$\Delta H^{\ddagger}$ (Kcal.mole^{-1})	$\Delta S^{\ddagger}$ (cal.mole^{-1}deg^{-1})
$-CH_3$	10.35 ± 0.02	-33.2 ± 0.2
$-CD_3$	10.26 ± 0.02	-33.6 ± 0.2
$-CH_2CH_3$	10.53 ± 0.04	-34.5 ± 0.4
$-CD_2CD_3$	10.49 ± 0.03	-34.7 ± 0.4
$-CH(CH_3)_2$	10.68 ± 0.05	-36.5 ± 0.6
$-CH(CD_3)_2$	10.62 ± 0.07	-36.7 ± 0.9

TABLE XI

EMPIRICAL PARAMETERS FOR THE SOLVOLYSIS OF SOME DEUTERATED AND NON-DEUTERATED TRIFLUOROACETATES IN H_2O

Ester	A	B
CF_3COOCH_3	-2261.9	3.0586
CF_3COOCD_3	-2243.0	2.9693
$CF_3COOCH_2CH_3$	-2301.9	2.7785
$CF_3COOCD_2CD_3$	-2292.1	2.7274
$CF_3COOCH(CH_3)_2$	-2335.4	2.3442
$CF_3COOCH(CD_3)_2$	-2322.1	2.2859

TABLE XII

RATE CONSTANTS† FOR THE SOLVOLYSIS OF TRIFLUOROACETATES AT 5°C, 10°C, 15°C AND 25°C*

Ester	T°C	k x 10^4 sec^{-1}
CF_3COOCH_3	4.963	23.42 ± 0.015
	10.007	33.45 ± 0.026
	15.001	46.51 ± 0.000
$CF_3COOCH_2CH_3$	5.001	8.837 ± 0.008
	10.002	12.69 ± 0.013
	15.000	17.69 ± 0.008
$CF_3COOCH(CH_3)_2$	5.001	2.465 ± 0.005
	10.000	3.554 ± 0.010
	15.001	4.993 ± 0.008
$CF_3COOC(CH_3)_3$	25.001	14.09 ± 0.007
CF_3COOCD_3	4.963	22.30 ± 0.015
	10.007	31.74 ± 0.016
	15.001	44.13 ± 0.016
$CF_3COOCD_2CD_3$	5.001	8.531 ± 0.004
	10.002	12.24 ± 0.015
	15.000	17.07 ± 0.019
$CF_3COOCH(CD_3)_2$	5.001	2.402 ± 0.007
	10.000	3.473 ± 0.0003
	15.001	4.844 ± 0.006
$CF_3COOC(CD_3)_3$	25.001	6.478 ± 0.053

† Average values
* Applicable only for tert-butyltrifluoroacetate

DISCUSSION

TABLE XIII

SECONDARY ISOTOPE EFFECTS FOR THE SOLVOLYSIS OF TRIFLUOROACETATES AT 5°C, 10°C, 15°C AND 25°C* (Using average rates)

Ester	Temperature °C	k_H/k_D
CF_3COOMe	4.963	1.050 ± 0.001
	10.007	1.054 ± 0.001
	15.001	1.054 ± 0.0004
CF_3COOEt	5.001	1.036 ± 0.0010
	10.002	1.037 ± 0.0016
	15.000	1.036 ± 0.0012
$CF_3COOiPr$	5.001	1.026 ± 0.0036
	10.000	1.023 ± 0.0027
	15.001	1.031 ± 0.0021
$CF_3COOtBu$	25.001	2.175 ± 0.018

* Applicable only for tert-butyltrifluoroacetate

The values for thermodynamic parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$) and solvent isotope effects (k_{H_2O}/k_{D_2O}) previously determined by Winter and Scott (29) clearly indicate that there is a definite shift in mechanism between the first three esters of the series viz. -Me, -Et, -iPr and the -tBu ester. The secondary deuterium isotope effects reported in Table XIII are broadly speaking in agreement with the conclusions of Winter and Scott (29). Although the values for the -Me, -Et and -iPr esters are small, there is a significant enhancement in the k_H/k_D ratio between -iPr and -tBu esters indicating a change in mechanism. The relevant data, on which these conclusions are based, is given in Table XIV.

The secondary deuterium isotope effects are all normal in the case of the trifluoroacetates. Llewellyn et. al. (94) investigated the α-deuterium isotope effect for the solvolysis of a series of methyl esters in water, with the methyl group fully deuterated. Their results are given in Table XV and it is to be noted that in these compounds the effects are uniformly inverse.

The authors (94) attributed inverse effects to stiffening of the C-H vibrations in the S_N2 type transition state, which produces a decrease in the zero-point energy level differences for the deuterium compound compared to the protium compound. This alteration dominates the change in the thermodynamic properties which arise from mass changes (translation and rotation) and consequently more rapid reaction of the light compound is favored. If the methyl halides, etc. give inverse isotope effects, methyl trifluoroacetate, which shows a normal isotope effect, presumably reacts by a mechanism other than S_N2. The secondary isotope effect is

TABLE XIV

THERMODYNAMIC PARAMETERS, SOLVENT ISOTOPE EFFECTS AND SECONDARY DEUTERIUM ISOTOPE EFFECTS OF TRIFLUOROACETATES AND t-BuCl IN WATER

Ester*	$\Delta H^{\ddagger}$ (H_2O) kcals/mole	$\Delta S^{\ddagger}$ (H_2O) e.u.	k_{H_2O}/k_{D_2O}	k_H/k_D†
-Me	10.35	-33.17	3.51	1.053
-Et	10.53	-34.50	3.61	1.037
-iPr	10.68	-36.49	3.79	1.027
-tBu	25.44	13.70	1.21	2.175
t-BuCl	23.79 (32)	14.41 (32)	1.38 (98)	2.45 (96)

† Average values at 10°C except -tBu, which is at 25°C

* k_H/k_D values reported are for $-CD_3$, $-CD_2CD_3$, $-CH(CD_3)_2$ and $-C(CD_3)_3$

Numbers in parentheses refer to literature references

TABLE XV (94)

DEUTERIUM ISOTOPE EFFECTS FOR METHYL COMPOUNDS HYDROLYSING IN WATER

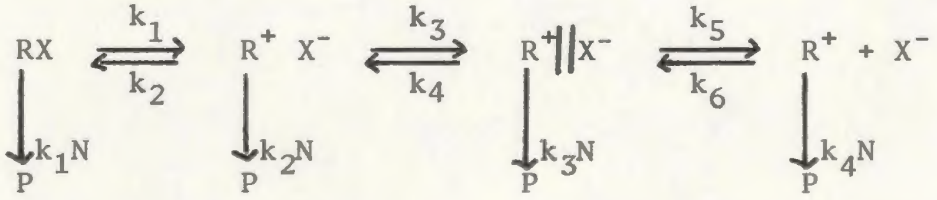
Ester	Temp. in ^{o}C	k_H/k_D
p-Methyl benzene-sulphonate	70.05	0.96
Chloride	89.794	0.92
Bromide	79.94	0.90
Iodide	70.05	0.87
Nitrate	100.005	0.92
Methanesulphonate	60.067	0.96
Methoxysulphonate	24.64	0.97

thus consistent with Bunton's (23) conclusion, that the hydrolysis of methyl trifluoroacetate takes place via a mechanism other than S_N2, most reasonably $B_{AC}2$. The ethyl and isopropyl trifluoroacetates give normal isotope effects, which roughly parallel those of Leffek and coworkers (95) for the solvolysis of structurally related alkyl halides. However, the entropies and enthalpies of activation for these esters together with the $k_{(H_2O)}/k_{(D_2O)}$ ratios securely place these substances in the $B_{AC}2$ category and hence the secondary isotope ratios for these substances do not provide a clearcut mechanistic distinction ($B_{AC}2$ versus S_N1-S_N2). The effect of deuteration, however, is less marked in the ethyl and s-propyl trifluoroacetates than in the corresponding halides, presumably a consequence

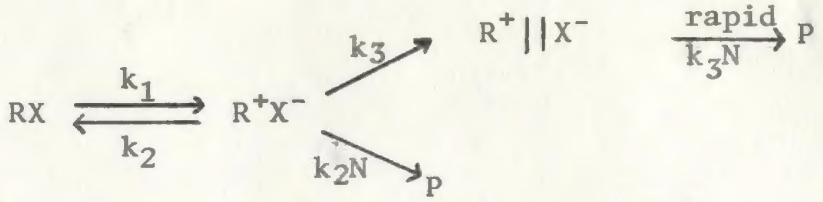
of the relative remoteness of deuteration from the reaction seat in the $B_{AC}2$ process.

The enhanced value of k_H/k_D = 2.175 for t-butyl trifluoroacetate, as compared to the values for the other three trifluoroacetates in the series, seems definitely to indicate a different mechanism for its hydrolysis. Such k_H/k_D values have been found for solvolysis of t-BuCl and t-Bu-d_9-chloride in water and other mixed solvents. Robertson et. al. (96) report a value of 2.45 in water at 20°C and Frisone and Thornton (97), values ranging from 2.30 in acetic acid-formic acid (29:71) to 2.46 in pyridine-water (51:49). The solvolysis of t-BuCl presumably takes place by an S_N1 mechanism and it seems logical to conclude that the t-butyl trifluoroacetate, which has a k_H/k_D of 2.175, must also be hydrolysing by an S_N1 mechanism, rather than a B_{AC} mechanism.

The most general mechanism for nucleophilic displacement of the previously labelled S_N1-S_N2 type is now considered to be (98):

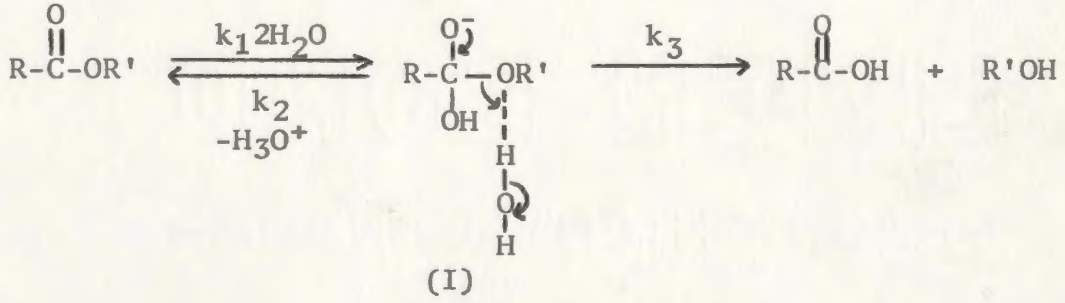


where $k_1 \longrightarrow k_6$ are the ionising components of the reaction and $k_1N \longrightarrow k_4N$ are the nucleophilic processes. The kinetically significant steps, in terms of this mechanism, represent the proper mechanistic question in the case of t-butyl trifluoroacetate. In a highly nucleophilic medium, such as H_2O, a truncated version of the above mechanism is probably



sufficient to explain the experimental results. The most important changes (geometrical changes, force constants, etc.) take place in the k_1 step, hence the largest isotope effect is probably on this step, the k_3 and k_2N steps involving smaller isotope effects. This is consistent with Frisone's and Thornton's (97) observations, since k_2N is the nucleophilic step and their isotope effect appeared to be independent of the solvent nucleophilicity. The magnitude of the isotope effect may be explained by hyperconjugation among the nine hydrogen atoms on the tertiary carbon atom or some sort of anchimeric assistance--hydrogen participation (59) from the same hydrogens, during any one of the steps of the mechanism.

The $B_{AC}2$ mechanism can be simply represented in the following manner:



Applying the steady state treatment for the formation and removal of the tetrahedral intermediate (I) we get:

$$\frac{d[I]}{dt} = k_1'[H_2O]^2[R\text{-}C(=O)\text{-}OR'] - k_2[I] - k_3[I] = 0$$

$$[I]\,(k_2 + k_3) = k_1'[H_2O]^2[R\text{-}C(=O)\text{-}OR']$$

$$\therefore \quad [I] = \frac{k_1'}{k_2 + k_3} [H_2O]^2 [R\text{-}\overset{O}{\overset{\|}{C}}\text{-}OR']$$

Now,

$$\frac{d}{dt} [RCOOH] = k_3[I] = \frac{k_1' k_3}{k_2 + k_3} [H_2O]^2 [R\text{-}\overset{O}{\overset{\|}{C}}\text{-}OR']$$

$$\therefore \quad k_{expt} = \frac{k_1 k_3}{k_2 + k_3} \qquad \text{where} \quad k_1 = k_1' [H_2O]^2$$

$$= \frac{k_1}{1 + k_2/k_3}$$

Let $k_2/k_3 = \alpha$ and if $\alpha >> 1$

$$k_{expt} = \frac{k_1}{k_2} \cdot k_3$$

$$= K_e \cdot k_3$$

For the protium compound,

$$k_{expt}(H) = K_e(H) \cdot k_3(H)$$

For the deuterium compound

$$k_{expt}(D) = K_e(D) \cdot k_3(D)$$

$$\therefore \quad \frac{k(H)}{k(D)} = \frac{K_e(H)}{K_e(D)} \cdot \frac{k_3(H)}{k_3(D)}$$

Since the carbonyl center is remote from the deuteration, we may assume that $\frac{K_e(H)}{K_e(D)} \simeq 1$, hence

$$\frac{k(H)}{k(D)} = \frac{k_3(H)}{k_3(D)}$$

On the basis of a naive zero point treatment with the condition that the vibrations of the methyl group do not alter when the ester forms an sp^3 intermediate, the assumption that the ratio $K_e(H)/K_e(D)$ approximates to unity is justifiable. This allows a discussion of the isotope effect entirely in terms of the rate constant k_3. The observed isotope effect is possibly a consequence of the net weakening of carbon hydrogen vibrations via hyperconjugation resulting from the increasing oxonium character of the alkyl oxygen atom when the second transition state is formed (equivalent to a β effect in S_N1-S_N2 displacements). The hyperconjugation hypothesis is also consistent with the observation that there is an overall reduction in the normal effect from the methyl to the isopropyl esters. However, if the postulate that deuterium can influence rates and equilibria by inductive as well as hyperconjugative effects is acceptable, it is important to discuss both of these possibilities in relation to the data reported here so that the above interpretations can be established with greater certainty. Furthermore, Leffek et. al. (99) have shown that γ deuteration relative to an incipient 'onium center gives rise to inverse effects and the significance of this fact with respect to the reduction of the isotope effect between the methyl, ethyl and isopropyl compounds merits examination.

The extension of the previous discussion commences with the recognition, that the ester alkyl group can interact inductively with the carboxylic center, thereby influencing k_1 and k_2 and hyperconjugatively with the incipient oxonium center, which arises from electrophilic attack at the oxygen atom linking the alkyl group to the trifluoroacetyl moiety of the substrate.

The structural change methyl $\longrightarrow$ methyl-d_3 should inductively decrease k_1 and increase k_2 leading to a normal effect for the ratio K(H)/K(D). However, in spite of the fact that the structural change ethyl $\longrightarrow$ ethyl-d_5 should inductively produce an increased decrement of k_1 relative to the methyl compound and greater increment in k_2, the net isotope effect is decreased. These considerations mean that the hyperconjugative influence on the ratio $k_3(H)/k_3(D)$ must dominate the overall effect.

It was pointed out earlier (99) that γ-deuteration produced inverse effects on certain carbonium ion* reactions. Such an effect might be invoked here to explain the reduction of the isotope effect between methyl, ethyl and isopropyl compounds. In terms of a zero-point treatment, an inverse γ-effect must involve some stiffening of the motions involving the deuterium atoms in this position. In the case of the carbonium ion reactions, the stiffening is postulated to arise from the stereochemical consequences of activation. These are best understood with the aid of the Newman projection diagrams I, II and III shown in Figure 7.

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*The designation, carbonium ion, here merely implies that the carbon atom undergoing substitution hybridises in the sense, $sp^3 \longrightarrow sp^2$ on activation. The substitutions in question, may have S_N2 transition states.

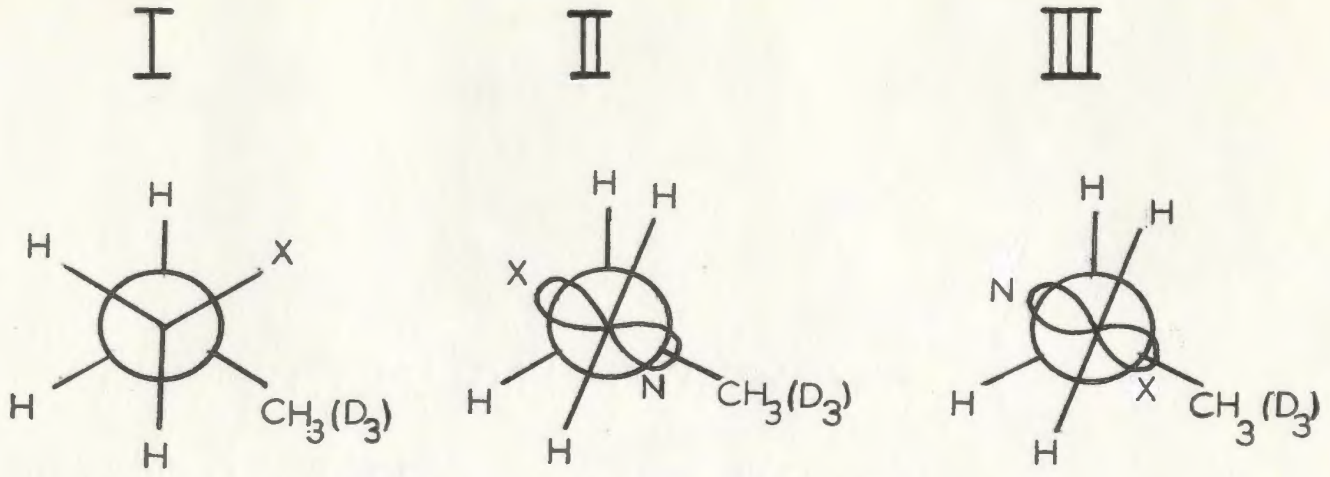

FIGURE 7.

In the transition states for these reactions, the lowest energy conformer will be that in which the most bulky group either N (attacking nucleophile) or X (leaving group) lies on a line, which bisects the angle between the two hydrogen atoms in the β-position. Irrespective of whether II or III represents the actual situation, either the departing group (X) or the incoming group (N) must eclipse the methyl group attached to the β-position. This suggests that the effect is primarily steric in origin and arises as a consequence of rehybridisation at the reacting carbon. In the case of the ethyl and ethyl-d_5 esters, as well as the isopropyl and isopropyl-d_6 esters, electrophilic attack at the alkyl oxygen atom will produce no extensive rehybridisation at this center, since the bond angles for di- and trivalent oxygen are quite similar and hence γ-effects of the sort appropriate to carbonium ion reactions are likely to be of less significance for the carboxylic ester hydrolysis.

Finally, it might be argued that the γ-methyl-d_3 in the ethyl-d_5 and isopropyl-d_6 might inductively increase the basicity of the oxygen

center. We rule out this possibility, since there is a reduction in the overall isotope effect from methyl-d_3 ⟶ ethyl-d_5 ⟶ isopropyl-d_6, whereas a steady accumulation of deuteriums should produce an effect in the opposite direction. However, the distinction between induction and hyperconjugation is not easily made in this series, since both effects would lead to the observed rate sequence.

REFERENCES

REFERENCES

1. J. Winter. MSc. Thesis. Memorial University of Newfoundland. September 1968

2. C. K. Ingold. Structure and Mechanism in Organic Chemistry. Bell and Sons Ltd., London (1953). Chapter XIV.

3. J. N. E. Day and C. K. Ingold. Trans. Far. Soc. 37, 686, (1941).

4. W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Mastermann and A. D. Scott. J. Chem. Soc. 1264, (1937).

5. L. R. C. Barclay, N. D. Hall and G. A. Cooke. Can. J. Chem. 40, 1981, (1962).

6. M. L. Bender. J. Am. Chem. Soc. 73, 1626, (1951).

7. L. P. Hammett. Physical Organic Chemistry. McGraw-Hill Book Company. New York (1940), p. 348.

8. M. L. Bender. Chem. Revs. 60, 54 (1960).

9. A. Moffatt and H. Hunt. J. Am. Chem. Soc. 79, 54 (1957).

10. A. Moffatt and H. Hunt. J. Am. Chem. Soc. 80, 2985 (1958).

11. A. Moffatt and H. Hunt. J. Am. Chem. Soc. 81, 2082 (1959).

12. E. Tommila. Ann. Acad. Sci. Fennicae, A59, No. 3, 3 (1942).

13. R. W. Taft, Jr. J. Am. Chem. Soc. 74, 2729 (1952).

14. E. D. Hughes and C. K. Ingold. Trans. Far. Soc. 37, 657 (1941).

15. E. K. Euranto and N. J. Cleve. Suomen Kemistilehti. 37B 5-6, 126 (1964).

16. E. K. Euranto and N. J. Cleve. Acta Chem. Scand. 17 (6), 1584 (1963).

17. E. K. Euranto and Anna Moisio. Suomen Kemistilehti 37B 5-6, 92 (1964).

18. E. K. Euranto. Acta Chem. Scand. 21 (3), 721 (1967).

19. E. K. Euranto. Suomen Kemistilehti B35, 18 (1962).

20. E. K. Euranto. Suomen Kemistilehti B33, 41, (1960).

21. M. Polanyi and A. L. Szabo. Trans. Far. Soc. 30, 508 (1934).

22. C. A. Bunton and Konasiewicz. J. Chem. Soc. 1354 (1955).

23. C. A. Bunton and T. Hadwick. J. Chem. Soc. 3248 (1958).

24. C. A. Bunton, J. N. E. Day, R. H. Flowers, P. Sheel and J. L. Wood. J. Chem. Soc. 963 (1957).

25. C. A. Bunton and D. N. Spatcher. J. Chem. Soc. 1079 (1956).

26. C. A. Bunton and J. L. Wood. J. Chem. Soc. 3043 (1957).

27. C. A. Bunton and T. Hadwick. J. Chem. Soc. 3043 (1957).

28. I. Talvik and M. Heinloo. Chem. Abstracts. 67:6343a.

29. J. G. Winter and J. M. W. Scott. Can. J. Chem. 46, 2887 (1968).

30. L. L. Schalager and F. A. Long. Advances in Physical Organic Chemistry. Academic Press Inc. (London) Ltd. Vol. 1, p. 1 (1963).

31. E. A. Moelwyn-Hughes, R. E. Robertson and S. Sugamori. J. Chem. Soc. 1965 (1965).

32. E. A. Moelwyn-Hughes, R. E. Robertson and S. E. Sugamori. J. Am. Chem. Soc. 87 2097 (1965).

33. R. E. Robertson. Solvolysis in Water, Progress in Physical Organic Chemistry. Vol. 4, p. 213-280. Edited by Andrew Streitwieser Jr. and Robert W. Taft, John Wiley and Sons, Inc., 1967.

34. A. Queen. Can. J. Chem. 45, 1619 (1967).

35. C. A. Bunton and V. J. Shiner, Jr. J. Am. Chem. Soc. 83, 3207 (1961).

36. P. M. Laughton and R. E. Robertson. Can. J. Chem. 34, 1714 (1956).

37. P. M. Laughton and R. E. Robertson. Can. J. Chem. 35, 1319 (1957).

38. P. M. Laughton and R. E. Robertson. Can. J. Chem. 37, 1491 (1959).

39. P. M. Laughton and R. E. Robertson. Can. J. Chem. 39, 2155 (1961).

40. G. Kohnstam. The Interpretation of Entropies and Heat Capacities of Activation in Solvolytic Reactions. The Transition State.

41. J. Bigeleisen. J. Chem. Phys. 17, 675 (1949).

42. L. Melander. "Isotope Effects on Reaction Rates," Ronald Press Co., New York, p. 15 (1960).

43. J. Bigeleisen and M. Wolfsberg. Advances in Chemical Physics, Vol. 1. Interscience Publishers, New York (1958).

44. E. A. Halevi. Progress in Physical Organic Chemistry. Vol. 1. Interscience Publishers, New York, p. 109 (1963).

45. E. S. Lewis and C. E. Boozer. J. Am. Chem. Soc. 74, 6306 (1952).

46. V. J. Shiner, Jr. J. Am. Chem. Soc. 75, 2925 (1953).

47. V. J. Shiner, Jr. J. Am. Chem. Soc. 76, 1603 (1954).

48. V. J. Shiner, Jr. J. Am. Chem. Soc. 78, 2653 (1956).

49. V. J. Shiner and J. S. Humphrey. J. Am. Chem. Soc. 85, 2416 (1963).

50. V. J. Shiner, B. L. Murr and G. Heinemann. J. Am. Chem. Soc. 85, 2413 (1963).

51. V. J. Shiner, W. Wilson, G. Heinemann and N. Solliday. J. Am. Chem. Soc. 84, 2408 (1962).

52. V. J. Shiner. J. Am. Chem. Soc. 83, 240 (1961).

53. V. J. Shiner, Jr. and C. J. Verbanic. J. Am. Chem. Soc. 79, 373 (1957).

54. E. S. Lewis and C. E. Boozer. J. Am. Chem. Soc. 76, 791 (1954).

55. E. S. Lewis and G. M. Coppinger. J. Am. Chem. Soc. 76, 4995 (1954).

56. E. S. Lewis, R. R. Johnson and G. M. Coppinger. J. Am. Chem. Soc. 81, 3140 (1959).

57. A. Streitwieser, R. H. Jagow, R. C. Fahey and S. Suzuki. J. Am. Chem. Soc. 80, 2346 (1958).

58. V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr and G. Lamaty. J. Am. Chem. Soc. 90, 418 (1968).

59. S. Winstein and J. Takahashi. Tetrahedron 2, 1316 (1958).

60. M. L. Bender, M. S. Feng and J. M. Jones. Chem. and Ind. 1350 (1959).

61. W. H. Saunders, S. Asperger and D. H. Edison. Chem.and Ind. 1417 (1957).

62. V. J. Shiner, Jr. Tetrahedron 5, 243 (1959).

63. E. S. Lewis. Tetrahedron 5, 143 (1959).

64. L. S. Bartell. Tetrahedron Letters No. 6, 13 (1960).

65. L. S. Bartell. J. Am. Chem. Soc. 83, 3567 (1961).

66. H. C. Brown, M. E. Azzaro, J. G. Koelling and G. J. McDonald. J. Am. Chem. Soc. 88, 2520 (1966).

67. G. J. Karabatsos, G. C. Sonnichsen, C. G. Pappaioannou, S. E. Scheppele and R. L. Schone. J. Am. Chem. Soc. 89, 463 (1967).

68. J. G. Jewett and R. P. Dunlap. J. Am. Chem. Soc. 90, 809 (1968).

69. V. J. Shiner, Jr. and G. S. Kriz. J. Am. Chem. Soc. 86, 2643 (1964).

70. A. Streitwieser, Jr. and R. C. Fahey. Chem. and Ind. (Lond.), 1417 (1957).

71. Belanic-Lipovac, Borcic and Sunko. Croat. Chem. Acta. 37, 61 (1965).

72. E. A. Halevi. Intern. J. Appl. Radiation and Isotopes 7, 192 (1960).

73. R. E. Weston. Tetrahedron 6, 31 (1959).

74. R. P. Bell and I. Coop. Trans. Far. Soc. 34, 1209 (1938).

75. J. W. Simmons and J. H. Goldstein. J. Chem. Phys. 20, 122 (1952).

76. E. A. Halevi. Tetrahedron. 1, 174 (1957).

77. E. A. Halevi. Tetrahedron 5, 352 (1959).

78. E. A. Halevi and M. Nussim. Bull. Research Council Israel. Sect. A, 5, 263 (1956).

79. E. A. Halevi and M. Nussim. Bull. Research Council Israel, Sect. A, 6, 167 (1957).

80. J. A. Dixon and R. W. Schiessler. J. Am. Chem. Soc. 76, 2197 (1954).

81. A. Streitwieser, Jr. and H. S. Klein. J. Am. Chem. Soc. 85, 2759 (1963).

82. A. Streitwieser, Jr. and H. S. Klein. J. Am. Chem. Soc. 86, 5170 (1964).

83. E. A. Halevi, M. Nussim and A. Ron. J. Chem. Soc. 866 (1963).

84. E. J. Bourne, M. Stacey, J. C. Tatlow and R. Worrall. J. Chem. Soc. 3268 (1958).

85. V. J. Shiner, Jr. J. Am. Chem. Soc. 74, 5285 (1952).

86. R. F. Nystrom, W. H. Yanko and W. G. Brown. J. Am. Chem. Soc. 70, 441 (1948).

87. J. B. Hyne and R. E. Robertson. Can. J. Chem. 35, 623 (1957).

88. E. A. Guggenheim. Phil. Mag. 2, 538 (1926).

89. R. E. Robertson. Can. J. Chem. 33, 1536 (1955).

90. H. C. Brown, D. H. McDaniel and O. Hafliger. Determination of Organic Structures by Physical Methods, edited by E. A. Braude and F. C. Nachod. Academic Press, Inc., New York, 1955. Chapter 4, p. 729.

91. D. G. Ives. J. Chem. Soc. 731 (1933).

92. G. Gorin, O. R. Pierce and E. T. McBee. J. Am. Chem. Soc. 75, (5622) (1953).

93. C. A. Bunton and T. Hadwick. J. Chem. Soc. 943 (1961).

94. J. A. Llewellyn, R. E. Robertson and J. M. W. Scott. Can. J. Chem. 38, 222 (1960).

95. K. T. Leffek, J. A. Llewellyn and R. E. Robertson. Can. J. Chem. 38, 2171 (1960).

96. L. Hakka, A. Queen and R. E. Robertson. J. Am. Chem. Soc. 87, 161 (1965).

97. G. J. Frisone and E. R. Thornton. J. Am. Chem. Soc. 90, 1211 (1968).

98. S. Winstein, P. E. Klinedist, Jr. and G. C. Robinson. J. Am. Chem. Soc. 83, 885 (1961).

99. K. T. Leffek, J. A. Llewellyn and R. E. Robertson. J. Am. Chem. Soc. 82, 6315 (1960).